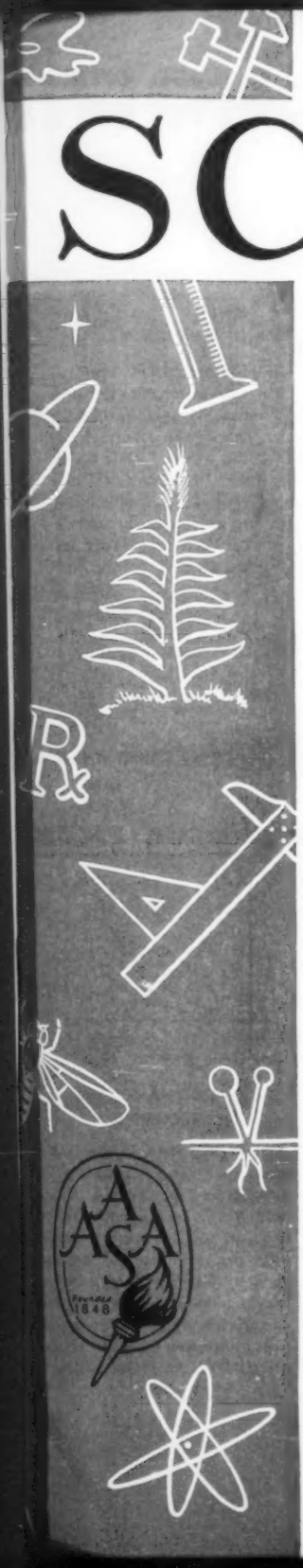

SCIENCE

AUGUST 7, 1953

VOLUME 118 NUMBER 3058

Contents

Research Planning and Research Policy: Scientists and Administrators: *Charles V. Kidd* 147

News and Notes

Mechanism of Enzyme Action: *B. L. Horecker* 152

Technical Papers

Avoidance Conditioning with Brief Shock and No Exteroceptive Warning Signal: *Murray Sidman* 157

An Apparatus for Centrifugation and Washing of Particulate Matter in a Controlled Atmosphere: *G. R. Mandels* 158

The Inhibitory Action of Hydroxylamine on Biological Oxidations: *Isaias Raw* 159

Intragastric Temperature Variations in Man During Hunger: *H. B. Benjamin, Marvin Wagner,* and *Walter Zeit* 160

A New Cytological and Histological Fixing Fluid: *Earl H. Newcomer* 161

Comparative Effects of Total Body Radiation, Nitrogen Mustard, and Triethylene Melamine on the Hematopoietic System of Terminal Cancer Patients: *R. Kenneth Loeffler, Vincent P. Collins,* and *George A. Hyman* 161

Aural Detection of Grain Infested Internally with Insects: *R. E. Adams* et al. 163

Estrogenic Activity of Isoflavone Derivatives Extracted and Prepared from Soybean Oil Meal: *Edmund Cheng* et al. 164

The Reduction by Reactivating Light of the Frequency of Phenocopies Induced by Ultraviolet Light in *Drosophila melanogaster*: *Max Perlitsh* and *Albert Kelner* 165

Comments and Communications

Eric Larrabee; J. P. Schafer; William S. Shore; and *Charles Tanford* 167

Scientific Book Register 168

Current Personnel Selection Procedures 3

Meetings & Conferences 18

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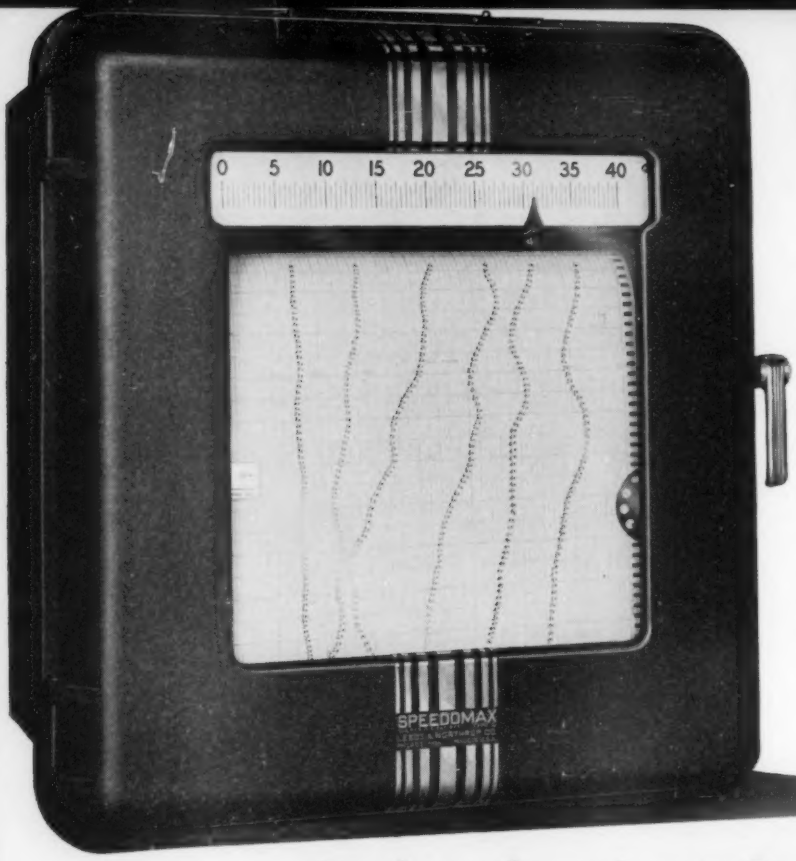

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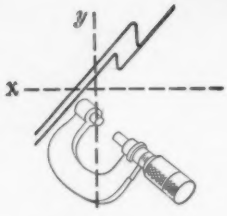

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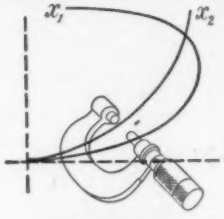

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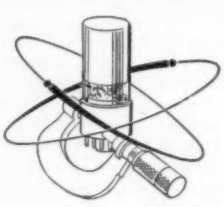

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Current Personnel Selection Procedures

A psychological test provides a systematic means of drawing inferences about individual differences in behavior. From a sample of behavior in the test situation it can be predicted how individuals will react in other circumstances. To establish the validity of the predictions, the test is tried out on persons of known competence.

Jephthah, wanting to distinguish his followers from the Ephraimites, knew that only his group could pronounce "sh." Having each man say "shibboleth," he effectively selected his men. This was a good test—short, objective, and perfectly valid.

Today our educational system, civilian and military government, and industry use tests by the millions. All are making predictions as to the later success of the individual. Although such forecasts rarely attain Jephthah's accuracy, they can be appreciably better than chance.

Personnel selection is based upon various combinations of tests, ratings of education and experience, appraisals of personality characteristics by interviews, and personal investigations. For other than routine jobs, there is frequently an interview of top-ranking prospects by persons with whom the employee will work. The relative emphasis upon different examining devices should depend upon their availability, practicality, and validity. For thousands of applicants, inclusion of a validated test battery may be wise. With no more than ten competitors, to limit the examination to committee ranking of application forms and brief interviews may be most feasible.

Interviews, as a component of the formal civil service examining procedure, present problems. Even with rigorous standardization, they remain subjective. To achieve comparable standards among boards is almost impossible. For many competitors, the cost is prohibitive. Moreover, ratings on interviews are difficult to defend upon appeal.

For many government positions below grade GS-11, applicants who meet minimum qualifications take tests. They are ranked by the tests alone or by these combined with a rating of education and experience. For positions at GS-11 and above, often the ranks are based only on the latter. In either case, the top three candidates are referred to an operating agency. It makes a selection or, with cause, may reject all three. For higher-level jobs, many agencies wisely make provision to interview the candidates, if budgets will permit, before making a probationary appointment.

Before World War II, the government's examining procedures were stagnant. The advances in vocational testing to meet war demands are well known, as witness the selection of airplane pilots. Faced with large-scale civilian personnel selection, during the war and immediately thereafter, the U. S. Civil Service Commission made more improvements than in the previous 20 years. Industry, too, has made rapid strides. New personnel consulting firms have developed, staffed largely from military testing programs. Even before the war, larger industrial firms were developing extensive personnel selection programs.

The Honorable James C. Worthy, Assistant Secretary in the Department of Commerce and formerly with Sears, Roebuck and Company, recently made an address on the government career service which has been interpreted in some circles as indicating opposition to tests. Those familiar with the testing program being fostered in the 600-odd retail outlets of Mr. Worthy's company and with his own interest in tests may well believe that he was exaggerating a possible misuse of tests to strengthen a plea for greater administrative latitude in selection of top personnel. Since knowledge and ability are never the sole components of job success, consideration might advisedly be given to some modification of selection methods for higher-level positions. This should not entail decrease in the use of tests for the purposes for which they are suited, for there must be assurance that career employees possess requisite skills and abilities. Nevertheless, individual differences in these characteristics within, say, successive tenths of the group who exceed minimum qualifications probably are not significant as compared with differences in other traits not measured by the tests. Enabling an administrator to choose for an important job from among the top ten per cent of qualified applicants rather than from among the top three might provide an effective supplement to the objective test and the rating of education and experience. Such a plan would add to selection costs, but perhaps not out of proportion to the gains.

DOROTHY C. ADKINS

University of North Carolina

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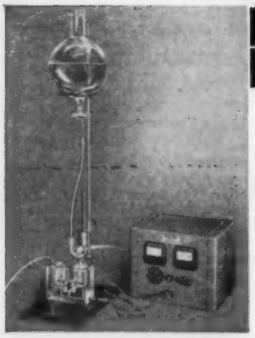

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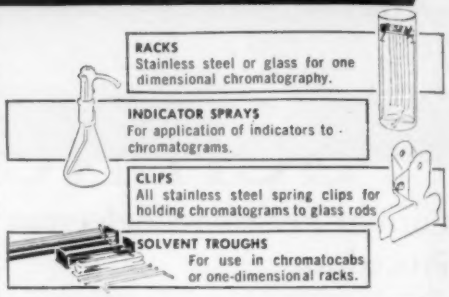

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1. Miller, C. O., A. E. Siehrs, and F. G. Brazda, Glucuronic Acid as a Growth Factor in Guinea Pigs, Proc. Soc. Expt. Biol. & Med., 30, 636-38, 1932-33.
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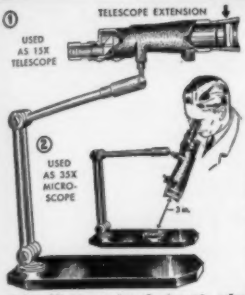

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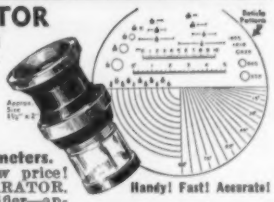

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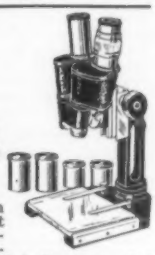

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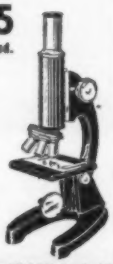

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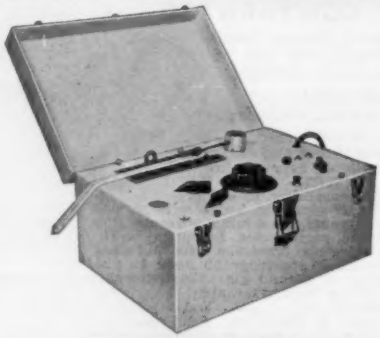

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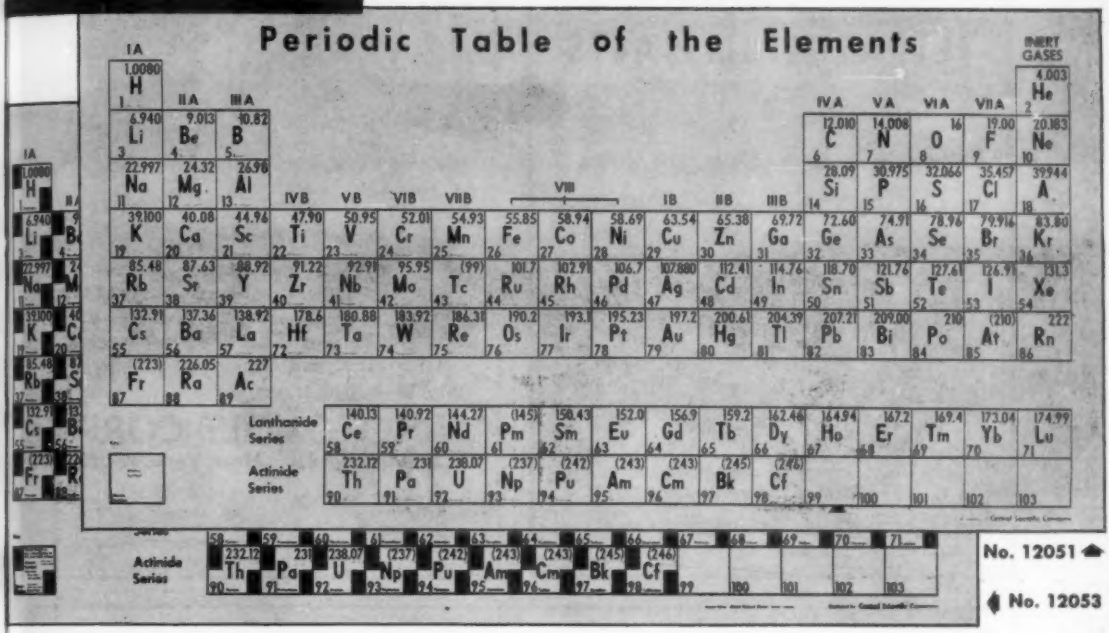

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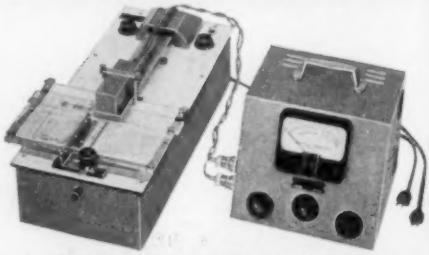

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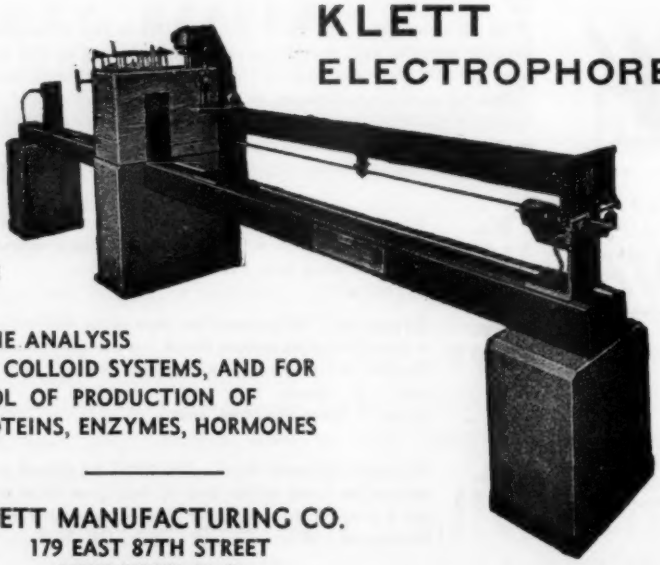

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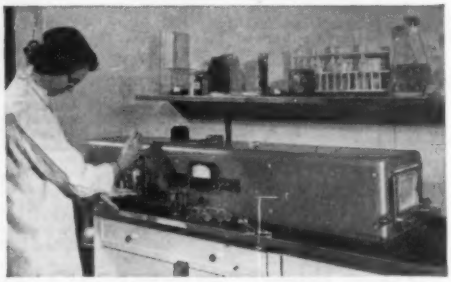

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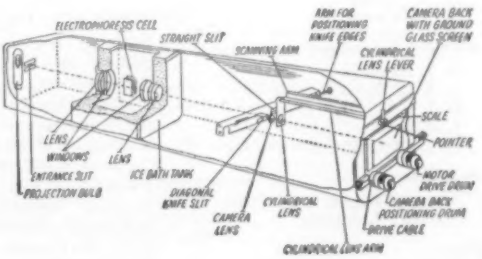

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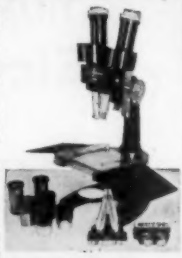

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Research Planning and Research Policy Scientists and Administrators

Charles V. Kidd

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. . . The proceeding upon somewhat conceived in writing doth for the most part facilitate despatch: for though it should be wholly rejected, yet that negative is more pregnant of direction than an indefinite, as ashes are more generative than dust.

—FRANCIS BACON, "Of Despatch"

ONE of the central dilemmas of research is reconciliation of the intellectual freedom required for effective exploration of the unknown with the selection and direction of effort implicit in the functioning of any organization with defined functions or limited resources. The concept of "research planning" is one aspect of this dilemma. This paper explores some aspects of the problem, some ways in which untoward consequences of the dilemma can be minimized, the meanings assigned to research planning by different groups, the kinds of planning appropriately done by these groups, and the interrelationships among various kinds of research planning. It also points out some of the issues that arise when the planning function appropriate to one group is undertaken by another, or when one group fails to recognize the nature of and necessity for planning by another group. Since these questions are complicated, the emphasis is on the interrelationship among different kinds of planning, rather than on the content of planning at any one level.[1] Finally, while the observations on which this discussion is based relate primarily to government, some of the problems seem common to the planning of research in industry and universities.

Consequences of Limited Concepts of Research Planning. One may say that a concept of research planning that encompasses decisions made by people or groups quite remote from a laboratory is nothing but an exercise in semantics, and that even if the idea is sound it has no particular use. However, there are important tangible and unfortunate consequences of any limited concept of research planning, whether it be a concept of research planning limited to the framing and execution of a set of experiments or a concept of research planning as the determination of general relative emphasis upon areas of investigation and the allocation of men, materials, and facilities. Some of these consequences can be profitably outlined before the kinds of research planning that take place in the laboratory and elsewhere are discussed.

[1] See D. C. Marquis, "Research Planning at the Frontiers of Science," *The American Psychologist*, Oct. 1948, p. 431, for a discussion of research planning in terms of three levels —experimental design, program design, and policy design.

If a scientist does not understand and accept the fact that he cannot rationally expect to be a free agent in any absolute sense, the result is likely to be resentment that can impair both his work and that of people whose job it is to plan for a more productive sum total of the work of all investigators.[2]

Investigators sometimes incline to lump together all decisions affecting their work but not made by them as "administration," and to view "administration" either as irrelevant or as an impediment to their work. This is not, of course, an attitude confined to people engaged in performing experiments. The director of a laboratory or a set of laboratories, for example, may deplore many "administrative" decisions made by those who have some degree of authority to plan his actions. These "administrative" decisions may be made by such groups as a board of trustees, a board of directors, or the Bureau of the Budget in the federal government.

Scientists whose work involves a great deal of administration sometimes seem reluctant to admit that they are "administrators" and tend to view themselves as "scientists" even when little of their time is spent on the substantive conduct or guidance of specific research projects. This may be because "administrators" and "administration" are held in relatively low esteem by substantial parts of the scientific community. Moreover, people with a heavy intellectual and emotional investment in the direct conduct of research are understandably reluctant to admit that they are leaving the field in which they have been specifically trained. Alan Gregg, among others, has deplored the fact that many good "research" men become "administrators": "The extraordinary feature of medical research in America in our times is the frequency with which demonstrated ability in research is rewarded by being extinguished. It would be consoling to think

[2] Some people who read this article in draft commented that, since scientists, like other people, generally recognize and accept forces beyond their control which affect their work, there is not much point in explaining what these forces are and how they operate. In the author's experience, however, the idea of scientific freedom is sometimes carelessly invoked to justify the position that any limitation upon scientists' freedom to determine what they will work on and what resources will be devoted to the work is wrong in principle.

that only in the earlier stages of institutional development is it necessary to sacrifice research to administration, and that once the preliminary planning has been done, men selected and trained to do research will find a tradition and circumstances facilitating their natural tastes and aptitudes. But the evidence about us hardly justifies such an evasive hope" (*1*).

But, if administration is viewed as research planning on a broad scale—as the development of scientific strategy, as the evolution of a consistent philosophy of research, and as the difficult task of bringing a sound philosophy to bear upon the conduct of research—there may be no net loss to research when a scientist turns administrator. Is not the resolution of such problems a task worthy of people who are scientifically trained, and a task that some scientists are uniquely equipped to perform? Is it not possible that in deploring the loss of scientists to administration one can lose sight of the facts that administration is more than a business management, logistics, and semiclerical functions and that science therefore has a tremendous stake in proper administration?

One may be skeptical of the productivity of research on the scale that now prevails in this country, but the situation exists. If the maximum return on the investment is to be secured, there are vitally important aspects of research planning that should be undertaken by minds of the highest caliber, sensitivity, and purpose.

The kind of limited concept of research planning that is potentially most dangerous is one which views the function as concentrated in groups outside the laboratory. If "administrators"—a department head, a laboratory director, an industrial executive, the Congress—fail to realize that there is an area and kind of planning that must be left to those actually engaged in research, the consequence is sterility of research. In the extreme, a concept of planning that overemphasizes the elements of planning that go on outside the laboratory leads to "master plans" that seem to be characteristic of authoritarian states.

The preceding observations on the kinds of planning decisions that take place in and out of the laboratory seem fairly obvious. Then what accounts for the undoubted fact that differences of attitude and tensions sometimes mark the relationship between persons engaged in different aspects of the planning of research? A full answer to this question would require a fairly extensive treatise on the philosophy of research, theories of group identification, and the theory and practice of administration. But some general sources of the problem can be briefly sketched. One of the sources of the problem is the tendency for persons at each level in a bureaucracy to consider themselves and those in their hierarchical class—laboratory chiefs, office of the secretary, bureau chiefs, deans—to be the level at which true wisdom and balanced perspective are concentrated.[3] That level is also often considered the one at which the really important decisions are made. Actions taken higher on the ladder are sometimes considered essentially unproductive maneuvering that can reach merely "administrative" or "political" ends. They often appear to be taken by persons whose actions are misguided or irrelevant and whose mission seems to be to impede, curb, and delay. Those actions taken lower on the ladder are often regarded as the commendable efforts of zealots upon whom the productivity of the organization depends, but who simply cannot or will not understand the full range of influences that must be taken into account in making the broader decisions.

When these attitudes develop, as they sometimes do, they are generally accompanied by the attribution of somewhat stereotyped personal characteristics to those in other hierarchical classes. Those above are often regarded as somewhat deficient in specialized training and viewed with a mild sort of tolerance. Those below are often regarded as highly but narrowly trained, and viewed somewhat paternalistically.

Another source of the difficulty is a tendency at times to make an unrealistic and grossly oversimplified distinction between "scientists" and "administrators." There are people who do research at the bench and nothing else. They are clearly scientists and not administrators. But a large proportion of scientists engaged directly in research are responsible in varying ways and degrees for the work of others, and the discharge of these responsibilities constitute administration. On the other hand, there are people whose work is confined solely to such tasks as "preparing budgets" and "processing personnel actions." They are clearly administrators and not scientists. But many scientists in university and industrial as well as governmental laboratories have administrative duties which they must perform. They are administrators as well as scientists. When scientists or administrators overlook the fact that many people perform mixed functions, it becomes easier to sort people into "us" and "them" groups.

A strong "us" vs. "them" atmosphere in a laboratory can impede the communication and working relationships that are essential to effective planning of research. For example, if administrators view scientists as a group apart, they may be led to view administration as an end in itself and forget that their role is to facilitate research. The large group of people who have both scientific and administrative duties may deplore and slight their administrative work because of the low esteem in which these activities are often held. Scientists may fail to appreciate the relevance and importance of decisions which affect them but which they do not make and may therefore resent the fact that those decisions are made.

For all these reasons, an understanding and acceptance of the fact that research planning necessarily occurs on a number of levels is important to the prosecution of research.

There remains, however, a more significant and a more difficult question. What kind of planning is ap-

[3] This may help explain why "freedom of research" is sometimes invoked most often by persons who are quite authoritarian in their relationships with those over whose work they have some degree of control.

propriate at what levels? The remainder of this paper centers around the total research planning process from the laboratory to Congress.

Planning in the Laboratory. Investigators quite often confine the meaning of "planning" to the degree and kind of establishment of hypotheses, organization of work, and assignment of tasks that they feel essential to their work. If a person defines planning in this way, he must arrive at the conclusion that "planning" by anyone else for him can constitute nothing but ignorant interference. And, given this definition, he is right.

What determines the degree of freedom that an investigator should have to plan and carry out his work?

The general mission of the laboratory is significant. To the extent that this mission is restricted, some limits can properly be placed upon the kind of work which the investigator undertakes. For example, if the task of the laboratory is to develop devices or processes, the staff can properly be limited to this area and the planning of individuals must be within these limits.

In organizations where basic research is an important or sole mission of the laboratory, the competence of the investigator generally plays a relatively more important role as the mission of the laboratory as such becomes broader.

Individual investigators—subject to the qualification noted below—must be free to select the problems which they wish to work on, how they approach the problem, how they design experiments, and must be free to shift from one area of research to another. These decisions certainly constitute the most direct, precise, and tangible form of research planning. This freedom of the mature investigator is necessary in basic research to provide the environment within which his intellect and ingenuity can operate most effectively. Such freedom may seem superficially to lead to anarchy. In fact, however, the "free" decisions of the investigator are closely determined by the nature of his endeavor and by his training even when he is not subject to the direction of another person. Even when the investigator follows a pure hunch, his hunch arises out of his store of accumulated facts, principles, and relationships in his field. This knowledge is supplemented by an indefinable process that fruitfully synthesizes in his mind what appear to be unrelated elements of a problem. For this reason, freedom of the able investigator does not lead to miscellaneous puttering, but to an intellectual effort that is generally highly disciplined. The nature of science itself imposes elements of planning.[4]

The varying capability of individuals sets limits on freedom. Full freedom is not an immutable natural right of all investigators. There is at times a tendency to identify "the freedom of science" with the right of any investigator to complete independence. Freedom is predicated upon the exercise of mature judgment by trained minds. The freedom of individuals to plan their work is, therefore, not a "yes" or "no" matter but a matter of degree. The right of an investigator to freedom in his work, i.e., to plan his work and to receive the resources to carry it out, is earned by achievement. Junior investigators must learn techniques and develop competence by working in collaboration with persons who have demonstrated their ability before extensive freedom of action and resources can be profitably put at their disposal.[5]

This question is faced by industrial as well as governmental laboratories. "It is the general experience of those laboratories in which fundamental research is carried out that the individual scientist almost always decides what specific problems he will undertake. A corollary to this is that if the scientist is not capable of deciding for himself what he should do, the director will see that he is given work which is supervised more closely" (*2*).

For all these reasons, the work of most investigators is planned to a lesser or greater degree by other scientists who guide or direct them by reason of status, intellect, or personality. It is therefore somewhat unrealistic to talk of "scientists" as if they constituted a homogeneous group and to speak of planning in a laboratory as if each scientist has, or should have, an equal degree of freedom to plan his work.

Planning by the Laboratory Chief. Just as work is often planned for junior investigators, the plans made by senior investigators are made within a framework set by decisions which they influence but do not control. This set of decisions can be considered planning just as the design and execution of a specific experiment require planning.

One set of decisions affecting investigators must be made by laboratory directors in governmental and industrial laboratories, and their counterparts in universities. These decisions relate essentially to the deployment of resources—manpower, space, facilities, supplies—among competing staff demands. The decisions set limits within which the plans of project leaders and individual investigators must be laid.

The extent to which and the detail with which specific tasks are assigned to investigators or teams of investigators by laboratory chiefs varies widely among laboratories. In general, the greater the element of applied research and development, the greater is the extent to which specific tasks should be assigned to investigators. The more fundamental the work of a laboratory, the greater should be the degree of freedom to select work and to deviate from any predetermined plan.

For several reasons, these principles are easier to state than to apply. Distinctions between basic and applied research are useful conceptually, but hard to make in practice. There is sometimes a tendency for

[4] Polanyi has stated this proposition elegantly in a chapter, "The Example of Science" in his book, *The Logic of Liberty.*

[5] This, like other fairly broad assertions that the reader may notice, is probably true as a generalization, but not as an invariable rule. Part of the job of a laboratory director is to select younger men who can be given a free hand to work on unorthodox leads. The story of Banting, Best, and insulin is a case in point.

investigators engaged in "applied" studies to claim that they are engaged in "fundamental" research because of the vague stigma that some scientific circles attach to applied work, and because they wish to secure for themselves the freer hand that traditionally goes with fundamental research.

In this connection, if competent investigators must be left free to determine what they work on and how they proceed, how is it possible to determine in advance—to plan—the general areas within which a laboratory will operate without decreasing the quality of research?

The answer lies in large part in selecting for work in a special field men with the training, experience, and desire to work in that field. As a general rule, even those investigators who shift their general field of inquiry do not do so abruptly. This makes possible the deliberate initial direction of the nature of the work of a new laboratory without directing the work of individual scientists.

Careful selection of personnel cannot only permit a laboratory director to set a laboratory program while leaving individuals quite free, but can even reconcile a substantial degree of coordination, direction, and "team" research with individual freedom. "A large measure of freedom and individual initiative can be preserved, if the coordination be wisely directed by selecting for the team those whose interests and aptitudes have already led them toward the problem which is to be investigated. They can then be left to explore, as they will, their own sector, aided and guided by the related findings of others in the group, encouraged by the assurance that their discoveries will quickly become a part of a greater accomplishment than they could attain unaided. It is thus possible to direct research for a desired end, without losing those intimate satisfactions which come to the investigator who follows his curiosity until he acquires understanding" (*3*).

The power of most laboratory directors to shape the programs of their laboratories is probably more easily exercised while the laboratory is being staffed than at any time thereafter. After the laboratory is staffed, the director must rely primarily not upon his authority to hire—a task that is in general performed with relative ease and in an atmosphere where freedom of choice is available to all concerned—but upon his power to stimulate, challenge, guide, and coordinate. Turnover may help him, but restaffing of a laboratory as a means of research direction is likely to be a long-drawn-out process. This does not mean that an established laboratory is inflexible, but it does mean that the extent of a program change and the speed of a change are limited by very practical factors.

The fact that the laboratory chief sets limits upon the resources available to investigators is in no real sense "a denial of freedom of research" or "administrative interference with research." While it may be in the interest of productive research to leave the minds of competent investigators free, each investigator can hardly exert a valid claim to unlimited financial support because his vocation is scientific research. The difficult problem, of course, is to make the judgments of the laboratory chief as sound as possible. One of the most crucial problems faced by a laboratory chief is to determine the rate at which the area of freedom given to an investigator—and the manpower, supplies, equipment, and space made available to him—should expand.

With the rapid postwar increase in both the number of large laboratories and the total scientific effort of the nation, a shortage of persons with the training and experience required to make these judgments has developed. Many laboratories are just beginning to realize that it may be necessary to plan more consciously the development of executive talent for research.

The laboratory director can, if he has adequate training and intellect, make sound judgments only if he is able to assess not only the current or potential significance of work in progress or proposed, but also the personalities, competence, and potentialities of the scientific staff. Unless his communications with the scientific staff are open, the director will make arbitrary and poor decisions, or decisions will go by default.

Conant has pointed out in another context the kinds of decisions faced by the laboratory director. ". . . many scholars have continued to dig assiduously but unprofitably in exhausted mines. All of which is inevitable and trivial except when loyalties and traditions urge men to claim either that digging is a worth-while activity in and for itself, or that the yield from an exhausted vein is full of gold. It is at this point that the argument between 'science for science's sake' and social utility begins. It may soon degenerate into an argument for the continuation of a particular line of intellectual activity merely because this has once been a fruitful direction of adventure. The argument soon becomes an emotional defense by those who love the field in question and who endeavor to support their loyalty by an appeal to general principles of the sacredness of all knowledge" (*4*).

It takes two to make an argument, and the argument in Dr. Conant's case is usually between the individual investigator and someone with authority to determine the resources available to him—a laboratory chief in government or industry or a department head or a faculty committee in a university. These decisions are the heart of "research planning" by the laboratory chief. They are hard to make. If they can be judged right or wrong, the judgment can be made only in retrospect, only as a batting average and only in the form of another set of interim judgments.

Research Planning as an Executive Function—Governmental and University. Another set of decisions affecting research must be made by the secretary of a federal department, the head of an industrial enterprise, or the president of an educational institution. Executives in these positions must weigh the

deployment of resources available to them, but their interests must center around the emphasis to be given to the research function as compared with other functions for which they are responsible, and the broad areas of emphasis of the research program.

Stated generally, "each step upward in the administrative hierarchy . . . should involve decreased concern with the concrete problems of research and increased concern with the more abstract problems of choice of facilities and of research programs" (*5*).

The way in which these problems of emphasis and choice are resolved constitutes a broad research plan, since the decisions fix the total scope of the research to be undertaken. In most federal agencies, the budget is the point at which the judgments are made final and effective.

But the problem is faced by universities, foundations, and industrial concerns as well as governmental agencies. For example, one of the broad choices to be made in guiding the general course of a university is to determine the relative emphasis to be placed upon the extension of knowledge, the conservation of knowledge, and the diffusion of knowledge. A determination of the emphasis to be placed upon extension of knowledge through research involves a deliberate choice among alternative courses of action. Specifically, the conditions under which a university will accept or reject gifts, the policies it will follow with respect to the volume of research grants or contracts that it will accept, determination of departmental budgets, establishment of general guides as to the kind of research that the institution will undertake, and selection of faculty constitute research planning on a relatively broad scale.[6]

Research Planning in Relation to Public Policy. The general planning decisions of individuals or groups responsible for specific research programs in industry, universities, and the government are in turn affected by forces which they may influence but which they do not control. At this stage, the idea of "planning"—already progressively attenuated through successive levels of decision making—virtually disappears. One is here in the area of the climate of public opinion toward science, general public understanding of science, the general place of science in our society, the schemes of values of large groups of people, and the broad political and economic forces that affect the volume and nature of research.

"Planning" in this area, if planning exists, is selection of national goals in the broadest sense. The planning process, if it exists, is the evolution of public opinion, and opinion in the scientific community, on general issues affecting science. One of these issues, indeed, is the extent and manner in which science can or should be "planned" nationally.[7] Another is the balance between secrecy and free communication, or between freedom of thought and behavior dangerous to the national security, that is best calculated to advance science and the national welfare. A third is the broad division of effort between applied research and development and fundamental research. A fourth is the proportion of the federal budget and of the national income properly devoted to research.

Attitudes toward and actions affecting these and other equally important issues affecting science as reflected in actions can be called "national science policy." In this sense, national science policy is as complicated and elusive as national policy in any other area of major concern to the country as a whole—foreign policy, agricultural policy, or management-labor policy. The issues seem amenable to discussion, clarification, and action not as a global whole but as separate but related areas.

At this level, the scientist reenters the planning scene as a citizen (*6*).

The Links Between Different Levels of Research Planning and Kinds of Research Planners. In this complex system for arriving at different kinds of decisions relevant to science, ranging from the design of specific experiments to quite general issues of public policy, there seem to be two particularly important conditions that must be fulfilled if the system is to work reasonably well. The first is maintenance of adequate communication between groups with different research planning functions. The second is the formulation of specific kinds of decisions at the level where competence and authority to make the decision are concentrated.

With respect to communication, the path must be open for the transmittal of the implications of research findings to the points where general decisions are made. To be specific, findings with respect to new weapons must be interpreted to those who lay strategic plans, and who determine procurement policy for the armed forces. In less applied fields, the potentialities of alternative areas of investigation must be communicated effectively to the points where budgetary decisions are made. Perhaps more important than communication of technical information is the existence of an understanding of the power of the experimental approach and of the conditions under which science will flourish or languish. Unless a substantial block of administrators has this understanding, the transmission of specific information is to a large degree meaningless. Indeed, decisions at higher administrative and political levels do not for the most part deal with the implications of specific findings—the early history of the atomic bomb project to the contrary notwithstanding—but with the general scale, the general areas, and the general conditions of scien-

[6] The establishment of a Committee on Institutional Grant Policy by the American Council on Education is an interesting example of the research planning process on this broad scale. The Committee's *Preliminary Report* (American Council on Education, Washington, D. C., Feb. 14, 1953) proposes a number of concrete policies which, if accepted, will constitute a form of research planning by universities.

[7] For expression of sharply divergent views on this complicated and highly controversial question see: Michael Polanyi, "The Planning of Science," *Pol. Quart.*, **16**, No. 4, 324–5 (1945); R. B. Goldschmidt, "Research and Politics," *Science*, **109**, 219 (1949); J. D. Bernal, *The Social Function of Science*. New York: Macmillan (1939).

tific endeavor. This certainly appears true with respect to the attitudes and level of understanding of the general public, which have a powerful and pervasive influence on science.

With respect to formulation of decisions at the appropriate level, a shrewd observer has said, "There is more inadequacy in government because of the inability of officials to operate on their proper levels than from any other single cause" (*7*). This is as true in the area of research as it is in other fields.

Trouble is ahead when an individual attempts to make decisions that people "above" or "below" him are more competent to make. Specifically, if the head of an agency makes a habit of dictating specific lines of experimentation, he is likely to destroy the effectiveness of the laboratory. This is true even though his judgment in some scientific areas may be superior to that of the staff. In other words, he is, or should be, restricted in the kind of research planning that he can productively engage in. Much of the fear of scientists engaged directly in research is based not upon the exercise of research planning functions by administrators, but upon apprehension that they will not confine themselves to appropriately general decisions. This apprehension is not always unfounded.

Whereas the making of detailed decisions by those who should confine themselves to general decisions is pernicious, an attempt by those appropriately concerned with detailed decisions to make general decisions is bound to be frustrating and futile. For example, the head of a laboratory cannot properly or profitably take upon himself the responsibility for indicating how much of the total federal budget should be allocated to medical research, even though he may have firm convictions on the matter. He can indicate what he believes to be a proper level of operation for the programs he heads, but he cannot assess the full array of factors that should influence the decisions of the secretary of his department, the Bureau of the Budget, and Congress.

It would, of course, be quite useful if one could formulate a set of criteria indicating precisely the kinds of decisions that people at a given level should and should not make. However, any attempt at precision in this area is almost certain to be a meaningless exercise because the nature of organizations, the content of research, and personalities vary so widely that what may be most productive in one situation may be quite disruptive in another.

One generalization that does seem sound, however, is that persons engaged in research planning should, in making decisions, or in refraining from making decisions, bear in mind not only the substantive merits of a question but also the level at which they act. If this consciousness of role were invariably present, common sense, reasonable sensitivity, and knowledge of the organization would substitute admirably for a set of precise guides.

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News and Notes

Mechanism of Enzyme Action

The Symposium on Mechanism of Enzyme Action, sponsored by the McCollum-Pratt Institute, was held at the Johns Hopkins University, Baltimore, June 16–19, 1953. This symposium, concerned with the fundamental problems related to the mechanism of enzyme action, was a logical and necessary extension of the previous symposium on Copper Metabolism, held in 1950, and the two symposia on Phosphorus Metabolism, held in 1951 and 1952. The symposium was organized, under the skillful guidance of W. D. McElroy and his associates in the McCollum-Pratt Institute, to follow a gradual and smooth progression from a consideration of electronic and ionic forces to group transfer mechanisms.

The first two days of the symposium were devoted to the more theoretical aspects of protein structure and the nature of the forces which bind protein molecules with each other and with smaller molecules. In the session on Protein Configuration and Biological Activity, J. G. Kirkwood discussed the forces between protein molecules in terms of a theory of matching constellations of charges. According to this concept, fluctuating distributions would, by induction effects, give rise to patterns specific for the interacting proteins. The nature of the essential groups for enzyme catalysts was considered by R. Herriott, who reviewed the evidence for the participation of specific functional groups in enzyme reactions, with particular emphasis on the appearance of such groups when inactive enzyme precursors, such as chymotrypsinogen, are converted to the active form. The first session was concluded by W. Kauzmann, who discussed the re-

versible and irreversible changes accompanying denaturation of proteins and enzymes and the properties which may be used to define a protein in its native state. In the second session, on the Kinetics of Enzyme-Catalyzed Reactions, H. Eyring covered kinetic and thermodynamic aspects, including the relation between reaction rates and activation energy and the possible effects of environmental influences during protein synthesis. H. Bull reviewed the role of the enzyme substrate complex as an intermediate in enzyme-catalyzed reactions, with particular emphasis on the kinetic treatment of reactions involving activators and inhibitors. In the third session, on the Function of Metals in Enzyme Catalysis, the theory of chelation and the relation between structure and binding affinity was reviewed by M. Calvin. The properties of metal protein complexes and the nature of groups in protein molecules responsible for the binding of metal ions were discussed by I. Klotz. E. L. Smith and his collaborators reported the results of studies with two highly purified metal peptidases, prolidase and leucine aminopeptidase, where a detailed study of metal and substrate specificity has permitted a number of conclusions regarding the binding mechanisms between substrate, metal activator, and enzyme.

In the last two days of the symposium attention was directed to a number of transport and transfer mechanisms. The fourth session, on the Mechanism of Electron and Hydrogen Transport, was opened by F. H. Westheimer, who reviewed the evidence for one-electron and two-electron transport mechanisms in oxidation-reduction reactions and the problem of free radical formation. The formation of enzyme-substrate complexes in living cells was demonstrated by B. Chance, whose elegant spectrophotometric methods have permitted the direct observation of reactions involving peroxidases, cytochromes, and pyridine nucleotide enzymes in intact cells. Evidence for the direct transport of hydrogen in reactions catalyzed by pyridine nucleotide dehydrogenases and for the steric specificity of such reactions was presented by B. Vennesland.

The final session included papers on the function of enzymes in group transfer reactions. The vast field of carbonyl and acyl group formation and transfer was reviewed by E. Racker, with special emphasis on the role of the sulfhydryl group in acyl transfer and of thiamine pyrophosphate in carbonyl transfer. I. C. Gunsalus provided an up-to-date discussion of the function of lipoic acid in the oxidation of pyruvate, with new evidence for its role as a carrier in oxidation-reduction reactions. A number of types of substitution mechanisms were discussed by D. Koshland, who illustrated the types of displacement reactions which are to be considered in an interpretation of enzymatic mechanisms. H. Kalckar reviewed the mechanisms of transglycosidation in the formation of polysaccharides and nucleotides and the role of uridine-containing coenzymes in such reactions.

Unfortunately the list of discussants, many of whom presented brief but nevertheless important original contributions, is too long to be included. The moderators, M. Heidelberger, F. Brink, L. Hellerman, E. G. Ball, and F. Lipmann, are to be commended for their part in leading the active and stimulating discussion which followed each paper. This discussion, faithfully recorded and transcribed by the McCollum-Pratt staff, should prove to be one of the most interesting features of the book, just as it has in past symposia. The critical exchanges between physical chemist, organic chemist, and enzymologist served to point up the important contribution which these branches of chemistry can make to biology. The forthcoming volume containing the symposium proceedings should be of great value to all concerned with enzyme studies.

As a consequence of the excellent arrangements, there was ample occasion for informal discussion and exchange of ideas outside of the meeting hall. The speakers, moderators, and especially the 85 invited discussants are greatly indebted to the sponsors of the symposium for making this opportunity available.

B. L. HORECKER

National Institute of Arthritis and Metabolic Diseases
National Institutes of Health

Scientists in the News

George A. Baitsell, Executive Secretary of the Society of the Sigma Xi since 1940, has resigned from that post and will devote himself to editorial duties for the Society. Dr. Baitsell, who is Colgate Professor Emeritus of Biology at Yale University, will be full-time editor of the *American Scientist,* the Society's quarterly, and of *Science in Progress,* the biennial volume. He has been editor of both on a part-time basis since 1940. In 1948–1949 he was also Editor-in-Chief of SCIENCE, **Thomas T. Holme,** Professor of Industrial Engineering at Yale, has been named Acting Executive Secretary to succeed Dr. Baitsell. A regular appointment will be made at the annual Sigma Xi convention in Boston next December.

John H. Cornehlsen, Jr., former scientist for the Department of Defense, has been elected Director of the Tufts Institute for Applied Experimental Psychology and Professor of Psychology at Tufts College. This position was previously held by **Leonard C. Mead,** who remains Chairman of the Department of Psychology and assistant for research projects to the president of the university. Dr. Cornehlsen's new duties will involve directorship of various projects being carried on at Tufts for government, industry, and private organizations in the fields of personnel, applied psychology, and human engineering. The Institute has a staff of 18 individuals with professional training. Its *Handbook of Human Engineering Data* is widely used by the armed forces and their engineering contractors in the development of equipment.

John E. McKeen, President of Chas. Pfizer & Co., Brooklyn, N.Y., has been awarded the Order of Vasco Nunez de Balboa, with rank of Knight Commander, by the Republic of Panama. The decoration is that country's highest civilian honor. Mr. McKeen, whose company is the largest producer of antibiotics, supervised the activities of the Pfizer research team which, in 1949, developed Terramycin. During World War II he was one of several American experts who, at the request of the U.S. Government, first developed procedures for the mass production of penicillin.

Gustavo Molina, Professor of Public Health Administration at the School of Public Health of the University of Chile, Santiago, has been appointed Chief of the Professional Education Branch of the Division of Education and Training for the Pan American Sanitary Bureau, Regional Office of the World Health Organization, Washington, D.C. Training professional public health workers holds a high priority in the international health services of the PASB.

The College of Physicians and Surgeons of Philadelphia has awarded the Alvarenga Prize for 1953 to **Francis D. Moore,** Surgeon-in-Chief, Peter Bent Brigham Hospital and Mosely Professor of Surgery, Harvard Medical School, for his outstanding contributions to our knowledge of the changes in body metabolism following surgery. The Alvarenga Prize was established by the will of DaCosta Alvarenga of Lisbon, Portugal, an Associate Fellow of the College of Physicians of Philadelphia, to be awarded annually by the College on the anniversary of the death of the testator, July 14, 1883.

Benedict Nagler, Chief of neuropsychiatric service at McGuire Veterans Administration Hospital at Richmond, Va., and Assistant Professor of Psychiatry and Neurology at the Medical College of Virginia, has been appointed Chief of the neurology section of the psychiatry and neurology division of the Veterans Administration in Washington, D.C.

H. L. Osterud retired July 1 after 31 years of service with the Medical College of Virginia as Professor of Anatomy. He was honored by a gathering of his friends and former students at which he received a bound volume of letters from his admirers, a radio-recorder and a gift certificate for records, and an all-expense paid two weeks' vacation in Puerto Rico made possible by MCV alumni in that country, and many personal tokens. Beginning next year a prize, known as the Osterud Prize, will go to a deserving student of anatomy. To fill the vacancy left by Dr. Osterud, **William M. Shanklin** has been appointed Visiting Professor of Anatomy. Dr. Shanklin comes to MCV from the American University of Beirut, Beirut, Lebanon.

Henry and Mary Paul, husband-and-wife biochemistry team at Eaton Laboratories, Inc., Norwich, N.Y., have been given new research positions. Henry Paul has been named Assistant Research Director and Mary Paul will take over her husband's former duties as Chief of the Biology Division. During the past decade the Pauls have conducted investigations into problems of cellular metabolism as part of the research program out of which the nitrofuran family of drugs has developed.

Captain C. P. Phoebus, MC, USN, has been appointed Special Assistant for Bio Sciences at the Office of Naval Research, Washington, D.C. A qualified naval aviator, Dr. Phoebus was Head of the Medical Military Specialties Branch and Aviation Medicine Section of the Research Division of the Bureau of Medicine and Surgery.

Maj. Gen. Donald L. Putt has been appointed commander of the Air Research and Development Command, whose headquarters are in Baltimore. Formerly vice commander of the ARDC, General Putt succeeds **Lt. Gen. Earle E. Partridge,** who has assumed his new duties as Deputy Chief of Staff for Operations, Headquarters, U.S. Air Force. The ARDC regulates the Air Force's integrated research and development program conducted at its nine research, development and testing centers located throughout the nation.

Burrell O. Raulston, Dean of the University of Southern California School of Medicine for ten years and a member of the faculty since 1929, has become Dean Emeritus. Dr. Raulston has been a resident of Southern California for 30 years and has long been prominent in medical education in the nation. He has been active in the Association of American Medical Colleges, the American Board of Internal Medicine, and the Councils of the U.S. Public Health Service. He was graduated from Maryville College and Rush Medical College, served in the Army Medical Corps in World War I, and then did graduate study at the University of Chicago, University of Bern, Switzerland, and Stanford Lane Hospital. In June Dr. Raulston was given an honorary degree of Doctor of Science by the University of Southern California at its 70th annual commencement exercises "in recognition of distinguished service in the field of medicine." He is succeeded by **Gordon Goodhart,** who has been on the SC medical school faculty for five years.

Frank Richardson, Chairman of the Department of Biology at the University of Nevada, has been dismissed by the Board of Regents. According to the President of the University, among the grounds for Dr. Richardson's dismissal was his distribution to his colleagues of copies of an article on certain aims and aspects of professional education written by Arthur E. Bestor, Jr., of the Department of History of the University of Illinois. The article, entitled "Aimlessness in Education," appeared in THE SCIENTIFIC MONTHLY of August, 1952. It calls for a restoration of emphasis upon intellectual content in the American curriculum, and decries the usurpation by the professional educators of the power of

making education policy. Dr. Richardson agreed with Bestor's point of view and used it to support his own position on local educational policies. (A later article, "Professional Education and the Disciplines," by William Clark Trow, Professor of Educational Psychology at the University of Michigan, presents the other side of the argument in THE SCIENTIFIC MONTHLY of March, 1953.)

M. W. Stout, President of the University of Nevada since September, 1952, and previously Principal of the University High School of the University of Minnesota, shortly after assuming office announced an entrance policy whereby the University would admit graduates of Nevada high schools who failed to meet regular entrance requirements, as well as non-graduates, if aged 21 and legal residents of the state. Such "unclassified students" would, it was hoped, make the necessary adjustment and work toward a degree. Dr. Richardson and certain other professors disagreed with this policy, which they felt seriously undermined academic standards.

On November 19 Dr. Stout held a conference with Harold Brown, Director of the School of Education, Dean Frederic Wood, and Dr. Richardson. Dr. Richardson gave his reasons for his actions. Then, in the President's own statement, it was pointed out that Dr. Richardson was hired to teach in the Department of Biology, and that the Administration would do everything it could to help him do a thorough job. Dr. Richardson was asked to return to his Department and devote his energies to his own work and not to interfere with the work assigned to other people.

As the president of his university's chapter of the American Association of University Professors, Dr. Richardson called a meeting to consider a questionnaire from the national office regarding administrative policies in universities and the participation of faculties in administration. President Stout thereafter called a faculty meeting, at which he charged that a minority of the faculty and some outsiders were working to endanger the University budget in the Legislature and were creating disloyalty and insubordination to the injury of the University. No one was named.

On March 31, Dr. Richardson, Assistant Professor Little of the same department, and three professors in the English Department were directed to appear before the Board of Regents to show cause why they should not be dismissed. Later the letters to Dr. Little and the English professors were rescinded.

After hearings, the Board of Regents dismissed Dr. Richardson. Two faculty members, one being Dr. Little, have since resigned. Dr. Richardson has appealed his case to the Nevada Supreme Court. The outcome of this litigation is awaited with interest. Other aspects of the story appear in *Time*, June 15 and 22.

Sir Robert Robinson of Oxford University, England, chemist, Nobel Prize winner, and an internationally known authority on vitamins, hormones, and other natural chemicals, will receive the American Chemical Society's Priestley Medal—highest honor in American chemistry—during the Society's 124th national meeting to be held in Chicago in September.

Education

Fifteen prominent scientific, industrial, and educational leaders have been named to a new advisory board created to assist **New York University's Institute of Mathematical Sciences.** A. B. Kinzel, President of Union Carbide and Carbon Research Laboratories, New York City, is Chairman of the group. Members of the board will assist the Institute in developing its facilities and will advise on problems of operation and administration.

NYU announced in January (SCIENCE, Feb. 6, 1953, p. 127) the creation of the Institute and the purchase of a nine-story building near Washington Square to house its activities. An outgrowth of the University's Institute for Mathematics and Mechanics, the Institute represents an expansion and integration of advanced research and instruction in the mathematical sciences. Some 150 persons will be employed at the Institute which will operate at an annual budget of more than one million dollars. A major facility in the Institute's building at 25 Waverly Place will be a computing center to be operated for the Atomic Energy Commission. The $880,000 Univac #4 is now being installed there.

Objectives of the Institute are to develop young scientists, of high caliber, to draw upon the experience of visiting professors and research scientists, and to combine basic research with instruction. David D. Henry, Executive Vice Chancellor of NYU, is Administrative Director, and Richard Courant, Professor of Mathematics, is Scientific Director.

Grants and Fellowships

A program of fellowships designed to prepare men for academic careers in medicine, principally in the field of pathology, has been established by the Department of Pathology in the University of Pittsburgh. The fellowships, entitled the **Sarah Mellon Scaife Fellowships,** will provide experience in research, teaching, and diagnostic pathology. Three years will be spent in the Department of Pathology, University of Pittsburgh. Arrangements will be made for one year to be spent at another medical center of the applicant's choice. One fellow will be appointed each for a four-year term and will receive a stipend increasing as follows: 1st year, $3000; 2nd year, $3300; 3rd year, $3700; 4th year, $4000. The applicant must be a graduate of an approved medical school. *Application must be made by November 1* for a fellowship beginning July 1 of the following year. Notice of selection will be made by December 15. Further information and application forms are available from Dr. Frank J. Dixon, Department of Pathology, University of Pittsburgh, Pittsburgh 13, Pa.

The **National Science Foundation** has entered into a contract with the Slavic Language Department of Columbia University, New York, to translate approximately 1,000 pages of current Russian research reports in physics during the coming year. The Columbia project is part of a larger program undertaken by the Foundation to make it easier for American scientists to keep informed of current scientific developments abroad. In the course of preparing translations the staff will also compile files of new or unusual Russian terms in physics and related sciences as the basis for an improved Russian-English scientific glossary. During the past year the Columbia group undertook preparation of a similar glossary of terms used in metallurgy.

Limited numbers of the completed translations will be printed at the facilities maintained at Oak Ridge by the U.S. Atomic Energy Commission. In addition to the official distribution to Federal agencies interested in the material, copies will be distributed to some 40 depository libraries throughout the country which hold complete files of AEC unclassified reports. Copies may also be purchased for a nominal charge at the Office of Technical Services, Department of Commerce, Washington 25, D.C. Titles will be announced in the *Bibliography of Technical Reports,* issued monthly by OTS, and in the *Monthly List of Russian Accessions,* issued by the Library of Congress. The translations concerning nuclear physics will also be announced in *Nuclear Science Abstracts.* The first group of translations will include physics reports from the January, 1953, issues of *Doklady Akademii Nauk SSSR* (Reports of the Academy of Science of the USSR).

Meetings and Elections

At its 2nd Annual Meeting the **American College of Cardiology** elected the following officers for the year 1953–54:

Pres.: Robert P. Glover, Clinical Professor of Surgery, Hahnemann Medical College and Hospital, Philadelphia, Pa.
Pres. Elect: Ashton Grayviel, Director of Research, U.S. Naval School of Aviation Medicine, Pensacola, Fla.
V. Presidents: David B. Dill, Hubert Mann, and John C. Krantz, Jr.
Sec.: Philip Reichert
Ass't. Sec.: Simon Dack
Treas.: Seymour Fiske
Ass't. Treas.: William L. Wheeler, Jr.
Trustees (for 2 years): Irving Brotman, George W. Calver, and Joseph P. Harvey

A **European Federation of Chemical Engineering** was formally inaugurated at a Foundation Meeting held in the Maison de la Chimie in Paris on the 20th of June, 1953. The purpose of this Federation is to promote European cooperation in the fields of chemical engineering and equipment. The Federation owes its origin to efforts commenced in 1951, and which assumed a more concrete form during the course of the European Convention for Chemical Engineering and the Achema X Chemical Engineering and Equipment Exhibition, which took place in 1952. These efforts have now been crowned with success. The following scientific and technical societies were represented at the inauguration of the Federation:

Asociación Nacional de Químicos de España, Madrid
Association des Ingénieurs et Techniciens Chimistes de Belgrade, Belgrade
Colegio de Ingenieros industriales, Madrid
Dechema Deutsche Gesellschaft für chemisches Apparatewesen, Frankfurt a.M.
Gesellschaft Deutscher Chemiker, Frankfurt a.M.
Instituto de Ingenieros Civiles de España, Madrid
Kemian Keskusliitto-Kemiska Centralförbundet, Helsinki
Nederlandse Chemische Vereniging, 's-Gravenhage
Sociedade Portuguesa de Quimica e Fisica, Oporto
Société de Chimie Industrielle, Paris
Société des Ingénieurs Civils de France, Paris
Schweizerischer Chemiker-Verband, Zürich
Schweizerische Gesellschaft für Chemische Industrie, Zürich
Schweizerischer Ingenieur- und Architektenverein, Zürich
Verein Deutscher Ingenieure, Fashgruppe "Verfahrenstechnik," Frankfurt a.M.

Many more scientific and technical societies, some of which are located in Norway, Denmark, Luxemburg and Austria, have signified their early intention of joining the Federation. The activities of the Federation are managed by a committee, and the following were elected members of this Committee of Management: Herbert Bretschneider, Germany; Hans C. Egloff, Switzerland; Francis A. Freeth, Great Britain; and Jean Gérard, France. The General Secretariats of the European Federation of Chemical Engineering are located in the Maison de la Chimie, 28 Rue Saint-Dominique, Paris, and in the Dechema-Haus, Frankfurt am Main, Rheingauallee, 25.

Officers of the **Illinois State Academy of Science** for the year 1953–54:

Pres: W. W. Grimm, Bradley University, Peoria
1st V. Pres.: G. W. Thiessen, Monmouth College, Monmouth
2nd V. Pres.: Lyle Finley, Monmouth College, Monmouth
Sec.: Lyle E. Bamber, Univ. of Ill., Urbana
Treas.: Walter B. Welch, So. Ill. Univ., Carbondale
Libr.: Thorne Deuel, State Museum, Springfield
Rep. on AAAS Council: Percival Robertson, The Principia, Elsah

Officers of the **Wisconsin Academy of Sciences, Arts, and Letters** for the year 1953–54:

Pres.: Charles L. Fluke, Univ. of Wis.
V. Pres. (Science): Henry Meyer, Ripon College
V. Pres. (Arts): Mary L. Doherty, Kenosha
V. Pres. (Letters): Harry H. Clark, Univ. of Wis.
Sec.: Robert J. Dicke, Univ. of Wis.
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Technical Papers

Avoidance Conditioning with Brief Shock and No Exteroceptive Warning Signal

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Experiments on avoidance behavior are usually divided, for the purpose of measurement, into trials. A trial, by definition, begins with the presentation of a warning signal and ends with the occurrence of the noxious stimulus or of the response which avoids the noxious stimulus. The measure, occurrence or nonoccurrence of the avoidance response, is necessarily a gross one since there are no intermediate states between the extremes. Traditionally, two expedients have been resorted to for circumventing this difficulty. Either the number of responses emitted by a group of organisms is averaged for each trial, or the trials for a single animal are grouped into blocks of arbitrary length and the number of responses averaged for each block. In the first case, a continuous measure is obtained only by virtue of the fact that progress is not uniform among organisms. The behavior of no individual can be described. With the second procedure, the type of relation obtained, if any, depends upon the number of trials included in each block. With both procedures, the statistical techniques result in the loss of a considerable amount of descriptive information. The purpose of the present paper is to report a technique which eliminates the above difficulties in investigating avoidance behavior, and to present an example of a kind of descriptive data which previous investigators in this area have generally neglected. Use of the rate measure, which is a natural one once behavior is freed from arbitrary constriction into trials, permits continuous observation and measurement of avoidance responding while providing a sensitive indicator of the effects of relevant variables (*1*).

White rats were the experimental organisms, with lever pressing selected as the avoidance response. Shocks of a fixed 0.2-sec duration were given to the animal through a grid floor at regular intervals unless the lever was depressed. Each lever depression reset the timer controlling the shock, thus delaying its appearance. If, for example, each lever press delayed the shock for 20 sec, a minimum interval of 20 sec was assured between avoidance behavior and shock. All other behavior was capable of being paired closely in time with the shock. Only the initial downward press on the lever reset the timer; holding the lever down had no effect upon the occurrence of the shock.

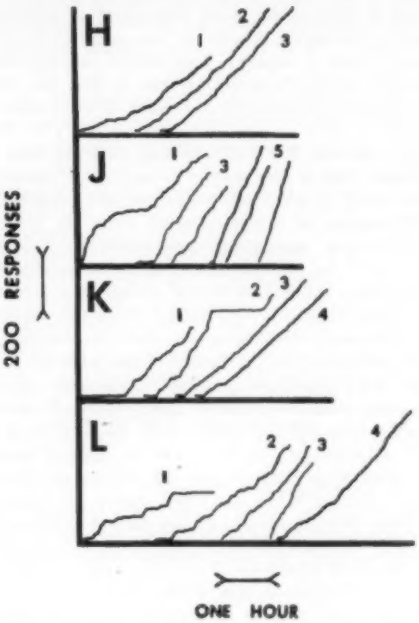

FIG. 1. Cumulative records of avoidance responding by 4 albino rats.

With no other contingencies between avoidance behavior and exteroceptive stimulation involved, approximately 50 animals have been successfully conditioned. Representative cumulated response curves for 4 of these animals are presented in Fig. 1. The letters refer to animals and the numbers to experimental sessions, each 3 hr in length. A striking characteristic of the initial curves is the abruptness with which the rate increases from its initial near-zero level. That these are not the unconditioned responses that hungry animals usually emit when the lever is first presented (*2*) was assured by making food and water continuously available to the animals in their home cages between experimental sessions, and by leaving the animals in the experimental cage, with the lever present, for 30 min before administering the first shock.

The initial curves are also characterized by their cyclic appearance and are composed of many small discontinuous segments. Responding of a more sustained nature is apparent as early as the final portion of the first session in some cases, but is most clearly demonstrated in later hours. With continued training the rate remains relatively stable not only within but also between sessions. Rates as high as 17 responses/min have been maintained by some animals during sessions totaling over 24 hr, with variations

[1] This paper is a portion of a dissertation submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the Faculty of Pure Science, Columbia University. The writer is indebted to William N. Schoenfeld and Fred S. Keller for their constructive criticisms.

no greater than 0.1 responses/min appearing between the average rate for each session.

The behavior generated by this procedure can be explained by a model which holds that avoidance responding increases in rate at the expense of other behavior that is depressed by shock. An equivalent statement, in reinforcement terms, is that the avoidance response is strengthened when it terminates incompatible behavior that has been paired with shock (*3*, *4*). Several lines of evidence indicate that the avoidance rate is not simply some form of temporal conditioning in which the responses are triggered-off by the passage of a time interval. Once the response has developed, each occurrence automatically varies the interval between shocks. Furthermore, the relatively stable rates that finally emerge are considerably higher than are required by the shock schedule. If a temporal discrimination were to develop, it should, according to previous findings with the white rat in other situations, produce much more efficient responding than is displayed here (*5*, *6*). Mitigating against a time discrimination, once the avoidance behavior appears, is the fact that the animal is provided with no indication that the end of an interval is approaching. While the shock can mark the start of a time interval of, i.e., 20 sec, once a response occurs this interval increases. It is, in fact, possible to vary the delay produced by each response, so that the amount of increase is completely unpredictable, even if the organism were to be provided with an internal resetting timer.

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An Apparatus for Centrifugation and Washing of Particulate Matter in a Controlled Atmosphere

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In the course of an investigation of the ascorbic acid oxidase of the fungus *Myrothecium verrucaria* it was desired to treat a suspension of spores with isoascorbic acid in the absence of oxygen and subsequently to wash the spores while still excluding oxygen. The apparatus described herein was devised and employed successfully for this purpose. A device of this type could find more widespread application and no comparable device has been encountered in the literature. The method can be used equally well for any gas mixture, and cells could be grown under pure culture conditions in the unit A-B. The apparatus is shown in Fig. 1. All joints are standard taper 24/40 with the exception of the male joint on B, which is shortened to a length of *ca* 15 mm so as to clear the centrifuge head. An aliquot of spore suspension is placed in tube A. The adapter B is then seated and the whole freed from oxygen by repeated evacuation and flushing with nitrogen through adapter C. With nitrogen in A, the stopcock on B is closed, adapter C is removed, and 1 ml of isoascorbate added to the well above the stopcock on B. Adapter C is then replaced and the isoascorbate freed of oxygen as above. While the isoascorbate is under vacuum, stopcock B is opened slowly, allowing the nitrogen in tube A to bubble slowly through the liquid to remove final traces of oxygen. Nitrogen is now re-admitted to the system, forcing the isoascorbate into tube A and the stopcock on B is closed. The centrifuge unit A + B is removed, incubated at 30° for 1 hr, placed in a 100-ml Cornell-style metal centrifuge tube, which is then filled with water to cushion the unit, and centrifuged 15 min at about 1000 rpm. Upon removal of the tube from the centrifuge, it is inverted and inserted in the open female joint in D of the washing apparatus D-E, the sedimented material remaining at the top of the tube. The chamber in D is freed

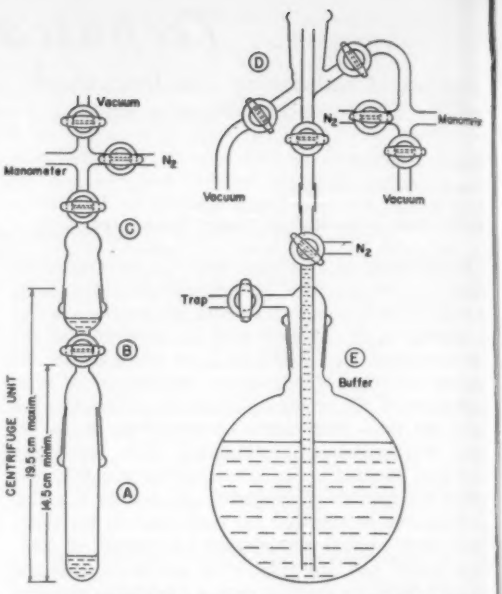

FIG. 1. Apparatus for washing cells in a controlled atmosphere by centrifugation; A–B, Centrifuge unit; C, Adapter for gassing centrifuge unit; D, Adapter for withdrawal of supernatant and admission of buffer; E, Reservoir of oxygen-free buffer.

[1] The author is indebted to Mrs. Gertrude E. Wagner for constructing the apparatus described, and to H. S. Levinson for critically reviewing the manuscript.

of oxygen. The supernatant, now being in B, is drawn off through the vacuum line after opening stopcock B. After flushing B and D with several changes of buffer, buffer is drawn into tube A and B, nitrogen is admitted to equalize the pressure, stopcock C is closed, and the centrifuge unit is removed. After shaking gently to stir up the sediment, the preparation is centrifuged and washed the required number of times as described previously. The centrifuge unit has been spun at 2200 rpm without breaking. Under these conditions the average relative centrifugal force was 900, and the maximum at the bottom of the tube was about 1500 times gravity.

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The Inhibitory Action of Hydroxylamine on Biological Oxidations

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Hydroxylamine is used as a reagent for acylphosphates (*1*) and acylmercaptans (*2*) and, in the concentration of 0.02 *M*, as a detecting agent for these compounds in enzymatic systems (*3*).

The oxidation of various substrates by rat liver mitochondria, isolated in isotonic sucrose, is strongly inhibited by 0.02 *M* of hydroxylamine.

TABLE 1

INHIBITION OF OXIDATION*

Expt	Substrate	O_2 uptake: Without	O_2 uptake: With NH_2OH	Time min	Inhibition %
1	*l*-Malic	99.5	50.3	30	49.5
2	Fumaric	31.5	12.6	15	60.0
3	Succinic	62.5	49.5	20	20.8
4	*l*-Glutamic	54.0	14.2	22	73.6
5	Succinic†	107.5	77.1	20	28.7
6	*l*-Glutamic‡	105.0	4.0	22	96.2

* Frozen Warburg vessels contained $MgSO_4$ 0.05 *M*, NaF 0.005 *M*, glycylglycine 0.02 *M*, adenosine-5-phosphate 0.004 *M*, orthophosphate 0.006 *M* pH 7.4, substrate 0.025 *M*, $NH_2 \cdot OH$ 0.02 *M*. Final pH 7.4. At 0 time 0.5 ml of mitochondria suspension in isotonic KCl. Gas phase air, temperature 20–25° C. Results are means of three or more flasks. Different substrates used with different mitochondria preparations.

† Enzyme aged for 15 min at 37° C.

‡ With 2,4-dinitrophenol 2.10^{-4} *M*.

Expts. 5 and 6 show that the inhibition remains even when oxidative phosphorylation is uncoupled by 2,4-dinitrophenol (DNP) or by aging at 37° C.

The inhibition is, at least, partly due to the combination with iron enzymes (*4*). In our conditions 0.02 *M* of hydroxylamine inhibited 100% the oxidation of added reduced cytochrome c, to mitochondria preparations.

Another point of inhibition exists, and it is shown by inhibition of the reduction of methylene blue in Thunberg tubes.

TABLE 2

INHIBITION OF DEHYDROGENASE SYSTEMS*

Substrate	Other conditions	ΔD, 660 mμ	$NH_2 \cdot OH$
l-Malic	—	34	4
Succinic	—	44	5
l-Glutamic	2.10^{-4} *M* DNP	44	2
l-Glutamic	15.10^{-3} *M* arsenate	36	2
l-Glutamic	Previous incubation with 1 mg riboflavin	47	3
Choline chloride†		90	5

* Thunberg tubes contain 2 ml orthophosphate buffer 0.125 *M* pH 7.4; 0.2 ml methylene blue 1/5000; 0.3 ml mitochondria suspension. In the sidearm 0.4 ml substrate 0.4 *M*. After evacuation and tipping, reaction was followed by direct reading at 660 mμ in Klett photocolorimeter.

† K_2HPO_4 0.01 *M* extract of guinea pig liver, instead of mitochondria.

No inhibition was found with crystalline alcohol dehydrogenase from yeast (*5*), nor with crude glutamic dehydrogenase from rat liver (*6*) measured by spectrophotometric determination of DPN reduction.

Diaphorase was prepared by the method of Edelhoch *et al.* (*7*), and its activity was measured in Thunberg tubes with methylene blue, diphosphopyridine nucleotide (DPN), and alcohol dehydrogenase. 2,6-Dichlorophenolindophenol cannot be used because it is reduced by hydroxylamine. Neotetrazolium confirms the results obtained by methylene blue, and it is not directly reduced by dehydrogenase-DPN, in absence of diaphorase. Hydroxylamine, in the same concentration, inhibited 90–100% diaphorase preparation before the alcohol step, but not after. The inhibition can be restored by the addition of alcohol insoluble protein. Trichloroacetic filtrate or boiled extract does not have this activity.

TABLE 3

INHIBITION OF DIAPHORASE*

Enzyme	Add	Direct reading 660 mμ: $NH_2 \cdot OH$ 0.02 *M*	Direct reading 660 mμ: —
Crude	—	9	79
Alcohol purified	—	86	85
"	0.2 ml alcohol insol. protein	8	84
"	Same & trichloroacetic filtrate	86	85
"	Same boiled 2 min	89	82

* In Thunberg tubes, 2 ml orthophosphate buffer 0.125 *M* pH 7.4; 0.1 ml alcohol dehydrogenase (100 units); 0.2 ml methylene blue 1/5000 0.1 ml diaphorase. 0.1 ml alcohol in sidearm. After evacuation and tipping reaction was followed by direct reading at 660 mμ in Klett photocolorimeter.

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Cytochrome c reductase activity of the same preparations is not inhibited by hydroxylamine. Hydroxylamine does not reduce reduced cytochrome c, These inhibitions must be kept in mind when using hydroxylamine as a trapping reagent.

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Intragastric Temperature Variations in Man During Hunger

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The temperature of an area of the body or an organ must be looked upon as variable. Regional temperature is dependent upon rate of blood flow, oxygen consumption, and heat gained or lost through outside influences. The emotional state of the individual, by causing sweating, blushing, or blanching, has a direct bearing on regional temperature, as the local vascular response is regulated by nervous impulses.

Tissue respiration is directly dependent upon blood flow. It is, therefore, important to think of the body architecture as physiological anatomy. In the light of rational and conservative body response, the blood requirements of an organ or tissue at rest would not be equal to the requirements of the same structure during the different degrees of activity. It becomes obvious, therefore, that shunting or bypassing should be a normal physiological phenomenon. Blood is diverted to the tissue or organ with the greatest need.

Since a change in temperature follows upon any regional change in blood flow, and therefore oxygen exchange, experiments were devised to demonstrate the relationship between the vascular pattern and intragastric temperatures. It seemed reasonable to suppose, therefore, that, if the blood volume and rate of flow to an area were increased, the temperature would rise; and that consequently, if the blood volume and rate of flow were reduced, the temperature in the area would fall.

For this study we made a thermopile of iron constantan wires threaded through a gum rubber tubing. The tips of the individual thermocouples were insulated with *sauereisen* and then covered with a rubber plastic. This thermopile was made up of eight thermocouples, separately insulated. The thermopile was conducted to a fixed cold junction in a Thermos bottle. Although these elements were insulated, they were immersed in an ice bath of distilled water. The Thermos bottle was grounded and the thermopile was connected by two leads, well insulated, to a specially constructed potentiometer with a 10-deg range and a 24-hr automatic recorder. The thermopile was then passed through the mouth into the stomach with little effort from the patient.

The position of the tip of the thermopile was checked by fluoroscopy. With the tube in place, the leads were attached to the potentiometer. The temperature of the cold junction was checked, and the potentiometer was activated. The moment the switch was released, the inked stylus automatically recorded on a circular rotating chart. The oral temperatures were taken periodically and charted (Table 1).

TABLE 1

Subject	Oral temperature (°F)	Initial intragastric temperature (°F)	Hunger-phase intragastric temperature (°F)
D.B.	98.6	101.0	98.8
R.H.	98.8	100.6	99.4
K.H.	98.6	99.8	98.8
J.W.	97.8	100.0	99.2
S.K.	98.6	100.6	99.2
R.B.	98.2	100.7	100.2
D.C.	98.0	101.0	99.3
B.M.	97.8	100.0	99.0

Our subjects were male and female first-year medical students. They were asked to register immediately prodromal symptoms of hunger and restlessness, and they were by and large quite cooperative.

As noted in Table 1, the oral temperatures consistently ran 1–3 deg lower than the intragastric temperatures. In our experiments it was noted that approximately ½ hr after the patient began to desire food, the temperature took a sharp dip to a lower level; shortly after the subject's "hunger pangs" had subsided, the temperature within the stomach returned to its previous plateau or near it.

It was postulated that this reaction took place because the muscular contractions of the stomach arrested the blood flow and led to a dearth of oxygen and a reduction of regional metabolism. This contention is based on the previously published work done at this institution on the neurovascular mechanism of the stomach (*1, 2*). It has been demonstrated that in the stimulated stomach the mucous membrane is kept in a state of anemia because of the shunting mechanism of the vascular bed.

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A New Cytological and Histological Fixing Fluid

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In the preparation of chromosomes for microscopic examination by the smear or squash technique, the Carnoy fixation[1] or one of its modifications is perhaps the most widely used by cytologists. It has, however, a number of disadvantages. The mixture should be freshly or at least recently made up before use; tissues cannot be stored in it for more than a few weeks; and, if it contains chloroform, the Feulgen reaction is inhibited with time. The frequent practice of storing materials in 70% ethanol after Carnoy fixation is, in our hands, only a desperate resort made necessary by the exigencies of the season or available research time and its use results in a rapid and steady deterioration of the stainability of the cells. As a result, the cytologist is the victim of a hectic cycle of feast and famine for research and teaching materials, and his choice of materials and prosecution of research are often seriously circumscribed.

This problem recently became acute with us during a study of avian chromosomes. Since only freshly killed material gave adequate staining reactions, the sacrifice of expensive birds at a frequency demanded by technical considerations might well have made the project too expensive for completion. An earlier effort to solve this problem by changing the staining combination (*1*), although an improvement, still left us with a chloroform-containing fixative which inhibited the Feulgen reaction and hardened the tissues after prolonged storage.

For these reasons a series of experiments combining a number of nonpolar or weakly polar organic compounds with propionic acid was run, using avian testes and 8-day-chick embryos as test materials for fixation. By an empirical process of examination, recombination, and elimination, the following formula (by volume) emerged: 6 parts isopropyl alcohol, 3 parts propionic acid, 1 part ether (petroleum), 1 part acetone, and 1 part dioxane.

This mixture is stable and can be made up in stock solution for use when needed, and it produces superb results. We have been using it in our laboratory for the past year in teaching and research and have found it eminently satisfactory for both plant and animal tissues. It has been used for avian testes, 40-hr and 8-day whole-chick embryos, the gonads of 4 mammals, grasshopper testes, and the following plant materials: *Tradescantia* and cucurbit microsporocytes, and root-tips of *Allium*, *Lilium*, and *Narcissis*. All the above materials, after storage in the fixative in the refrigerator at 4° C for periods of 5–11 months, are still staining sharply with propionic carmine and the Feulgen stain.

The time of hydrolysis for Feulgen in normal HCl at 60° C is 10 min for plant materials and 20 min for the animal tissues after prolonged storage.

With animal tissues the fixative is replaced once after 12–24 hr with fresh fluid, after which all materials are stored in the refrigerator until needed. These tissues can be either smeared directly or prepared for embedding in paraffin and the sectioning technique by replacing the fixative with absolute alcohol which is followed by xylol and paraffin. Thus all stages of dehydration save the one are eliminated, and we believe the fixation image is better than those usually produced by the conventional fluids containing salts of heavy metals. Furthermore, no bleaching is required prior to staining.

In preparation for hydrolysis for the Feulgen reaction, the tissues are washed for 1–2 hr, hydrolyzed, rinsed in distilled water, stained 2–3 hr in Feulgen, and smeared directly from Feulgen on the slide in a drop of 45% acetic acid. To make the Feulgen smear permanent, the slide is heated, pressure is applied on the coverslip, and the slide is immediately inverted in a Petri dish and covered with absolute alcohol to which fast green may be added for counterstain. When the coverslip comes off, it is immediately reunited to the slide with diaphane or euparal. The results, in our hands, are equivalent to any of the more complicated Feulgen procedures usually recommended in the literature. The same procedure may be used for making permanent preparations of propionic carmine smears.

[1] The original Carnoy fluid apparently consisted (by volume) of 6 parts absolute ethanol, 3 parts chloroform, and 1 part glacial acetic acid. Most investigators transpose the proportions between chloroform and acetic acid or omit the chloroform entirely.

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Comparative Effects of Total Body Radiation, Nitrogen Mustard, and Triethylene Melamine on the Hematopoietic System of Terminal Cancer Patients[1]

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Nitrogen mustard and allied agents have come to be considered as alternative agents for radiotherapy in the treatment of several forms of cancer. Comparable clinical regression of disease and similar histologic changes have led to the use of the term "radio-

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mimetic." Where both agents are of known effectiveness, nitrogen mustard is usually preferred for generalized disease because the dose of total body radiation is believed to be limited to an ineffective level by radiation sickness and bone marrow depression. At the same time, the anticipated nausea, vomiting, and profound hematologic changes which follow vigorous chemotherapy are considered justifiable, and recovery is known to be reasonably certain. Comparably severe effects have not been produced by doses ordinarily employed in total body radiation. It seems possible that tolerance and recovery from radiation have been underestimated. A study was therefore undertaken to compare the effects of nitrogen mustard and allied agents with the effects of increasing doses of total body radiation.

All patients had advanced cancer and were considered suitable candidates for chemotherapy. One patient was given 5 mg of methylbis (2-chloroethyl)-amine (HN_2) intravenously, one was given 5 mg of triethylene melamine (TEM) orally, and two received 50 r total body radiation. The x-ray factors were two million volts peak potential, target-skin distance 360 cm, filter 4 mm of lead, half value layer 6.6 mm of lead, air dose 50 r, skin dose 55 r, depth dose at 10 cm—41 r, and depth dose at 20 cm—23 r. In a second group, two patients were given 10 mg of HN_2, two were given 10 mg of TEM, and one received 100 r total body radiation under the same conditions as the previous group. When the patient receiving 100 r total body radiation failed to show any appreciable hematologic depression as a result of this treatment, one further patient was given 150 r total body radiation.

All patients studied received the following laboratory examinations before treatment: red blood count, hemoglobin, white blood count, differential count, reticulocyte count, platelet count, gastric analysis, bone marrow aspiration biopsy, plasma protein determination, serum bilirubin determination, plasma iron concentration, plasma iron turnover rate using Fe^{59} as a tracer, and red cell uptake of injected Fe^{59}. The iron studies were carried out because of the work of Huff, Hennessy *et al.* (*1, 2*). This demonstrated an effect of total body irradiation on the turnover of plasma iron and the utilization of this iron in the formation of red blood cells which appeared to be quantitatively related to the dose delivered.

These tests were repeated as frequently as was feasible following treatment. All patients were in a terminal state and it was not expected that the treatment would appreciably change the course of their diseases. None of the ten patients studied showed a deterioration in his condition that could be ascribed to the treatment given although several expired within a relatively short time thereafter.

Both chemotherapy and radiotherapy were given as single doses or exposures to eliminate the time factor. It is generally appreciated that higher doses are tolerated if radiation is given over a period of time (*3, 4*). The demonstration of higher tolerance levels of total body radiation may well prove of value in the management of diseases currently being treated routinely with nitrogen mustard and its derivatives.

All patients receiving nitrogen mustard or TEM developed malaise of varying severity, but none of the patients receiving radiation mentioned any changes in

TABLE 1

Patient	Disease	Treatment	RBC (millions)	Hb (grams %)	WBC (thousands)	Differential	Platelets (thousands)
W. B.	Carcinoma of lung	50 r	4.3 ā rx* N. C.	12 ā rx N. C.	6–8 ā rx N. C.	N. C.†	230–260 ā rx N. C.
J. F.	Carcinoma of colon	50 r	3.0 ā rx N. C.	9 ā rx N. C.	9–11 ā rx N. C.	N. C.	270 ā rx 90 at 2–3 wk
D. R.	Carcinoma of scalp	100 r	4.9 ā rx 4.0 at 6 wk	14 ā rx 11 at 6 wk	7–9 ā rx N. C.	N. C.	250 ā rx N. C.
R. F.	Carcinoma of sigmoid colon	150 r	3.4 ā rx N. C.	9 ā rx N. C.	7–9 ā rx 5 at 5 wk	N. C.	200–210 ā rx 100–130 at 4–5 wk
G. S.	Carcinoma of cervix uteri	5 mg HN_2	4.0 ā rx 3.0 at 16 days	9 ā rx 6 at 16 days	15 ā rx 8 at 3 wk	N. C.	300 ā rx N. C.
J. P.	Carcinoma of lip	10 mg HN_2	4.0 ā rx 3.3 at 31 days	12 ā rx 10 at 31 days	7–9 ā rx 5 at 18 days	N. C.	175–200 ā rx N. C.
M. B.	Carcinoma of vulva	10 mg HN_2	3.6 ā rx 3.1 at 23 days	10 ā rx 7 at 23 days	8–15 ā rx 7 at 23–30 days	12% lymph. ā rx 28% lymph. at 23–30 days	300–330 ā rx N. C.
J. A. H.	Carcinoma of prostate	5 mg TEM	4.2 ā rx 3.7 at 6 days	12 ā rx 10 at 6 days	15 ā rx N. C.	N. C.	210–240 ā rx N. C.
A. M.	Carcinoma of lung	10 mg TEM	4.5 ā rx 3.4 at 36 days	13 ā rx 9 at 36 days	11 ā rx 5 at 28 days	14% lymph. ā rx 5% lymph. at 7 days	170–200 ā rx N. C.
J. E. H.	Glioblastoma multiforme	10 mg TEM	5.1 ā rx N. C.	15 ā rx N. C.	9–11 ā rx N. C.	N. C.	180–210 ā rx N. C.

* ā rx before treatment.
† N. C. no significant change.

TABLE 1 (*Continued*)

Patient	Marrow aspiration	Other	Iron turnover rate (half-time in hr)	Plasma iron concentration (μg %)	Period of follow-up
W. B.	Hypoplasia ā rx* N. C.	N. C.†	1.0 ā rx 0.5 at 3 hr 1.1 at 7 days	65 ā rx 41 at 3 hr 40 at 7 days	5 wk died
J. F.	Normal ā rx N. C.	Free HCl: 55° ā rx 0° at 1 day 41° at 7 days	0.4 ā rx 0.5 at 3 hr 0.7 at 7 days	49 ā rx 43 at 3 hr 58 at 7 days	5 wk died
D. R.	Normal ā rx Hypoactive at 7 days	N. C.	2.0 ā rx 1.1 at 1 day 1.5 at 7 days	68 ā rx 112 at 7 days 89 at 51 days, 18 at 66 days	4 months living
R. F.	Normal ā rx Hypoactive at 7 days Normal at 36 days	Icterus: 2–5 ā rx 14 at 4 days 2–4 at 8 days	0.7 ā rx 0.7 at 1 day 7 days and 35 days	150 ā rx 75–85 at 1–23 days 150 at 29 days	3 months living
G. S.	Normal ā rx Greatly decreased at 21 days	N. C.	0.8 ā rx 0.8 at 1 day 3.0 at 8 days	93 ā rx 73 at 1 day, 59 at 8 days 45 at 17 days, 27 at 24 days	Deteriorating at 27 days signed out
J. P.	Normal ā rx N. C.	N. C.	1.1 ā rx 1.2 at 1 day 0.9 at 7 days 0.8 at 35 days	85 ā rx 75–100 at 1–36 days 38 at 44 days	4 months living
M. B.	Normal ā rx Increased cellularity at 15 days	N. C.	1.0 ā rx 1.1 at 1 day 0.6 at 8 days	85 ā rx 72 at 8 days 33 at 23 days, 85 at 38 days	4 months living
J. A. H.	Normal ā rx N. C.	N. C.	1.2 ā rx 1.2 at 1 day 1.2 at 7 days	123 ā rx 121 at 1 day 83 at 7 days	7 days signed out
A. M.	Normal ā rx N. C.	N. C.	0.7 ā rx 0.6 at 1 day 0.5 at 7 days 0.6 at 36 days	85 ā rx 55–65 at 4–30 days 47 at 36 days	3 months living
J. E. H.	Not done	Not done	1.1 ā rx 0.9 at 1 day 0.6 at 8 days	123 ā rx 82 at 1 day 115 at 8 days	11 days died

* ā rx before treatment.
† N. C. no significant change.

symptoms. One patient stated (J.F.) that he felt much better for 2 days following the treatment.

The data is summarized in Table 1. Except for the few changes mentioned specifically, there were no alterations in plasma proteins, serum bilirubin, reticulocytes, or gastric acidity.

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Aural Detection of Grain Infested Internally with Insects

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The detection of internal or hidden insect infestation in grains by electronic means was suggested before modern electronic techniques were available (*1*), but no useful developments of this kind have occurred. Our study of this application, which is one of a continuing series of investigations at this station aimed at developing inspection techniques for internally infested grain (2–5), has indicated that it may have considerable practical utility and, in addition, potentialities as a research tool for the insect physiologist concerned with the movement and feeding habits of insects which infest grain kernels internally.

The techniques and equipment are simple. The only major equipment requirement, in addition to a low noise level audio amplifier, a suitable microphone, and a loudspeaker, is a soundproof box. Our best results have been obtained with a concrete box having walls

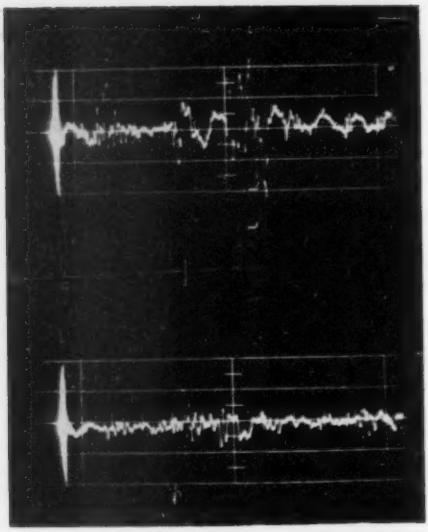

FIG. 1. Oscilloscope patterns of noises of internal infestation in wheat grains.

and removable cover 2½ in. thick, within which boxes of copper and Celotex surrounded the infested grain lying on the microphone. Records of wave patterns were made with a Tektronix oscilloscope and a Polaroid-Land camera attachment. Insects in the larval, pupal, and adult stages can be detected within the infested kernels, although the egg and extremely early stages of larval growth cannot. It appears that the larva must be nearly a week old before sufficient noise is produced for detection. In this research the stage of the infestation hidden within the grain kernels could be selected for study by means of x-ray techniques previously developed at this station (*3*).

Two distinct types of sound are associated with the larval and pupal stages, namely, a low-frequency scraping noise and a high-frequency tearing or rasping sound. From repeated observations it has been deduced that the low-frequency sounds are made by the movement of larva and pupa within the kernels, and the high-frequency sounds by the chewing of the endosperm of the grain by the larva. When several infested kernels are placed on the microphone, combinations of these frequencies may appear as shown in Fig. 1. Figure 1 was taken with the oscilloscope set at a sweep frequency of about 30 cps, and the insect sounds of both high and low frequencies are present. Thus in the upper trace the right and left ends show the low noise frequencies centering around 200 cps, characteristic of insect movement. Just to the right of the vertical scale in the center appears a high frequency burst of sound in the range of 1200–1500 cps. The frequency range of sounds due to internal insects appears to range from 200 to 8000 cps, although the lower limit has not been accurately determined. The voracious eating habits of the larval stage of rice weevil (*Sitophilus oryza* L.) has been clearly confirmed by this technique. It was also of interest to learn that, when the infested grains are disturbed in any way, the high-frequency sounds indicative of chewing usually cease and the low-frequency sounds, due apparently to movement, continue intermittently. After a short time the high-frequency sounds reappear. An experienced observer can estimate the approximate stage of development of the insect because the sounds are slightly different in the larval and pupal stages. This observation has suggested analysis of the recorded sound wave patterns as a means for differentiating developmental stages as well as physiological activities. Additional studies now in progress include evaluation of the method to determine numbers of infested kernels on the basis of cumulative recording of wave peaks, analysis of differences in sound characteristics of different species which infest grain internally, relationship of frequency of feeding and movement to stage of insect development, and determination of the influence of storage temperature and humidity on the nature, frequency, and periodicity of the sound patterns produced.

One practical application of this work is a means for the rapid evaluation of the effectiveness of fumigants whereby the normal delay of several weeks required for emergence of surviving insects, now necessary to determine fumigant efficiency, can be eliminated. A suitable sound detection device for performing such tests in mills and grain elevators is now under construction. Another application of the principle would be a means for monitoring grain within storage bins for infestation without sampling or removing the gain from the bins, in much the same manner as permanent thermocouple systems are now used for checking the heating of grain in storage.

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Estrogenic Activity of Isoflavone Derivatives Extracted and Prepared from Soybean Oil Meal[1]

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Implantation of diethylstilbestrol (synthetic estrogenic substance) pellets under the skin of cattle and sheep stimulates live-weight gains and increased feed

[1] Journal Paper No. J-2262 of the Iowa Agricultural Experiment Station, Ames, Iowa Project 1208.

efficiency during the fattening period (*1–3*). Recently, naturally occurring estrogenic substances have been detected in varying amounts in various plant herbages, both pasture and hays, fed to cattle and sheep (*4–6*). Genistein (5,7,4′-trihydroxyisoflavone) has been suggested by Curnow and Bennetts as the chemical constituent responsible for estrogenic activity in one of these herbages, namely, subterranean clover (*7*). The glucoside of genistein, genistin (5,4′-dihydroxy-7-glucosidoisoflavone) has been shown by Walter (*8*) to be present in substantial amounts (0.1%) in soybean oil meal. Since soybean oil meal is used rather widely in livestock feeding, it appeared advisable to investigate the estrogenic activity of both genistin and genistein in ascertaining their probable significance in livestock feeding.

Commercial soybean oil meal (solvent process) was extracted with methanol according to the method of Walter (*8*). Genistin was isolated as pale yellow, thin rectangular plates having a melting point of 256° C. Upon hydrolysis of genistin with hydrochloric acid in methanol, genistein was obtained. It was crystallized from hot 60% ethanol as white rectangular rods having a melting point of 298° C.

The estrogenic activity of these compounds was determined by the mouse uterine weight method described in detail in an earlier paper (*6*). The chemicals under study were either fed directly to immature female mice or were injected subcutaneously. Since neither genistin nor genistein is soluble in water, they were injected as their sodium salts. Six mice were used in each group, and the treatments were given once daily for 4 days. The mice were sacrificed 24 hr after the last treatment, their uteri dissected, fixed in Bouin's fluid, and weighed. The results obtained are presented in Table 1.

Feeding 2.5 and 5.0 mg of either genistin or genistein per day per mouse resulted in increased uterine weights. Injecting genistein at 1- and 2-mg levels respectively also increased uterine weights consistently over the corresponding weights of control animals. Whereas the injection of 1 mg of genistin did not have a measurable effect, the injection of 2 mg proved quite effective. It should be noted that these responses are similar to those due to the injection of 0.02–0.04 μg respectively of diethylstilbestrol, as shown in Table 1. The estrogenic activity of genistein can accordingly be estimated as approximately equivalent to 1/50,000 the activity of diethylstilbestrol. Genistin activity on a weight basis was slightly lower than that of genistein. However, the two compounds appeared to have approximately equal activity on a molecular basis.

Experiments are in progress with fattening lambs to determine whether the estrogenic activity of genistin as found in soybean oil meal is as beneficial as the estrogenic activity of stilbestrol, which has been shown experimentally to be valuable in lamb feeding. Although the estrogenic activity of genistin per unit of weight is small compared with that of diethylstilbestrol, the relatively large amount of genistin present in soybean oil meal, coupled with its presence in small amounts in certain hays, suggests the likelihood that the amounts present in certain cattle and sheep rations may be sufficiently large to exert major beneficial influences.

TABLE 1

ESTROGENIC ACTIVITY OF GENISTIN AND GENISTEIN

Group	No. of mice	Treatment*	Av uterine weight, mg
1	6	Normal control	9.7 ± 2.8
2	6	Feeding genistin, 2.5 mg	12.9 ± 4.4
3	6	Feeding genistin, 5.0 mg	39.8 ± 8.9
4	6	Injecting genistin, 1 mg	9.2 ± 1.7
5	6	Injecting genistin, 2 mg	14.6 ± 3.6
6	6	Feeding genistein, 2.5 mg	21.6 ± 13.4
7	6	Feeding genistein, 5.0 mg	22.6 ± 4.6
8	6	Injecting genistein, 1 mg	13.2 ± 2.4
9	6	Injecting genistein, 2 mg	17.0 ± 7.3
10	6	Injecting stilbestrol, 0.02 μg	13.2 ± 2.6
11	5	Injecting stilbestrol, 0.04 μg	18.3 ± 6.9

* Treatment was given daily for 4 days.

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The Reduction by Reactivating Light of the Frequency of Phenocopies Induced by Ultraviolet Light in *Drosophila melanogaster*

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Phenocopies (*1*), or abnormalities of adults simulating mutations, are readily induced in *Drosophila melanogaster* by irradiating eggs, larvae, or pupae with ultraviolet light (*ca.* 2600 A) (*2, 3*). Visible and near-ultraviolet light (3600–4900 A) prevents ultraviolet-induced killing or mutation in bacteria and other organisms (*4, 5*). Such reversal of ultraviolet effects has been found in various organisms (see [*5*] for references) including, recently, *Drosophila*, where reactivating light lowered the incidence of ultraviolet-induced lethal mutations (*6*).

It became of interest to determine whether phenocopies induced by ultraviolet light in *Drosophila* were also affected by reactivating light, especially since the induction of phenocopies was perhaps a more complex phenomenon than those studied before.

TABLE 1

EFFECT OF REACTIVATING LIGHT ON SURVIVAL AND ON THE INCIDENCE OF PHENOCOPIES IN ULTRAVIOLET-IRRADIATED PUPAE

No. of pupae	Ultraviolet light (min)	Reactivating light (min)	Percentage of pupae hatching	Percentage of phenocopies in adults
56	0	0	84	0
86	5	0	68	76.5
47	5	35	66	41.5
43	5	70	72	32.2
43	5	120	81.5	38.0

The L-S strain of wild-type *Drosophila melanogaster* was cultured on molasses-cornmeal-yeast-agar medium. Eggs laid in a 2-hr period were segregated and incubated at 25° C for 7 days. Immediately after pupation, pupae were distributed over the bottom of a dry Petri dish and irradiated with ultraviolet light from a 15-watt low-pressure mercury lamp (GE germicidal) emitting chiefly radiation at 2537 A. The pupae were irradiated for 5–7 min at 20-cm distance from the bulb, then immediately exposed for 30 min or longer to reactivating light from a 100-watt ribbon filament tungsten bulb. The reactivating light was cooled by passing it through 2 cm of water. Care was taken not to disturb the pupae between irradiations, to make certain that the same region of the pupae exposed to ultraviolet light was exposed to visible light. After irradiation, the pupae were exposed to diffuse room light for not more than 1½ min. The dish with the pupae was placed in a bowl containing a large food chip, the bowl was covered with gauze netting, and the pupae were incubated in the dark at 25° C until they hatched. "Dark" controls were treated similarly, except that they were not exposed to reactivating light after ultraviolet radiation. The adult flies were etherized and examined with a 20 × microscope. Any visible abnormalities in the flies were scored as phenocopies.

An ultraviolet dose was chosen which gave abundant phenocopies without decreasing survival markedly. A typical experiment is shown in Table 1. Reactivating light increased survival. The frequency of phenocopies in pupae treated with visible light was reduced to about half that of the "dark" control.

In the experiment shown in Table 1 any fly with an abnormality, whether severe or slight, whether in one area or in several, was scored as one phenocopy. But, if the average number of abnormalities per fly was taken as the measure of phenocopy induction, the effect of reactivating light was more pronounced than indicated in Table 1. In one experiment the average number of abnormalities per fly in the "dark" control was 1.78, many flies having three or four abnormalities, e.g., in the abdomen, wings, eyes, and bristles; in the reactivated group it was 0.65. In the latter group none of the flies had more than two areas of the body abnormal. Moreover, the severity of the abnormalities in the group treated with visible light was always less than in the "dark" control.

The types of phenocopies were, in general, similar to those reported in the literature, namely, distortion and irregular banding in the abdomen (a very common abnormality), abnormal wings, distorted eyes, missing, fused, or "singed" hairs and bristles. One-sided effects, similar to those found by Geigy (*2*) in which only one side of the animal was abnormal, were common.

Several experiments were made which indicated that the photoreversal of the induction of phenocopies was a phenomenon essentially similar to photoreactivation in bacteria.

Thus, if a glass filter (Corning No. 3385) cutting off wavelengths below 4700 A was interposed in the path of the light from the tungsten lamp, there was no reduction in phenocopies, whereas blue and violet light (obtained by the use of Corning filter 5850, transmitting only wavelengths below 4900 A) was effective. It should be noted that, contrary to our experience in photoreactivating bacteria, a GE AH-5 medium pressure mercury lamp was not a suitable source of reactivating light, since the radiation from this lamp was itself lethal to pupae. This lethality was perhaps due to the abundant radiation at 3650 A present in the AH-5 lamp.

Treating the pupae with visible light *before* ultraviolet light had no effect on phenocopies. If ultraviolet-irradiated pupae were allowed to incubate in the dark before exposure to visible light, the incidence of phenocopies was no longer reduced. After about 20 hr, visible light had little effect.

In summary, the ability of ultraviolet light of wavelength 2537 A to induce phenocopies in *Drosophila melanogaster* is markedly reduced by exposure to visible light. And, since the phenomenon appears similar to photoreactivation in bacteria, we may expect the same basic mechanism of action to be involved in both organisms.

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Comments and Communications

Two Spheres Collide

MR. ERIC LARRABEE (SCIENCE, **117**, 395 [1953]) warns us, in a rather wordy and opaque style, of the dangers of contemporary barriers between science and humanity, between scientists and people. His suggestion that where science fails to answer the demand for popular enlightenment, the "faddist and crank" will step in, seems unfortunately true.

However, SCIENCE readers should be reminded that only three years ago Mr. Larrabee, under the title "The Day the Sun Stood Still" (Harpers Magazine, January, 1950), made a strong plea for serious scientific consideration of Velikovsky's "Worlds in Collision," and in a later article Velikovsky had the last word on his critics.

The controversy over that extraordinary work of the imagination has almost entirely died down, and the judgment of scientists is admirably expressed in Dr. Laurence Lafleur's "Cranks and Scientists" (SCIENTIFIC MONTHLY, November, 1951). But we have a right to ask whether Mr. Larrabee still compares Velikovsky with Galileo and Copernicus, or whether he now relegates him to purgatory with L. Ron Hubbard and Gayelord Hauser. Is Mr. Larrabee a clear-sighted guide into the future, or a distressing example of past lack of comprehension?

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Received April 27, 1953.

DR. SCHAFER raises an issue which I discussed with the then editor of SCIENCE before the article appeared, since I knew that Mr. Meyerhoff disapproved of my attitude toward Velikovsky in equally vehement terms. On March 23, 1953, I wrote him as follows:

"It occurs to me, re-reading a few passages in it, that some readers may be annoyed at a presentation of such views without comment indicating that I have been associated with a man like Velikovsky, who is generally regarded as un-scientific. Those who remember my *Harper's* article, in other words, may feel that I am appearing here under false pretenses. As you know, I don't wish to make a point of that association, or intrude it into scientific publications unless so requested, but neither am I ashamed of nor anxious to conceal it."

Apparently it is necessary for me to explain that in spite of my "wordy and opaque style" I have no scientific credentials and do not presume scientific standing for my opinions. I did not compare Velikovsky to Galileo or Copernicus (nor did I consign Hubbard and Hauser to purgatory, for that matter). I did, however, make what amounted to a plea for serious consideration of Dr. Velikovsky's thesis, and I have not been persuaded to abandon that position by the criticisms of his books that have so far been published.

Since my views are requested, I can only state that the "attack" on Velikovsky seemed to me singularly unconvincing. Dr. Lafleur's article, which was the last of many, was also the first to make even a modest pretense of pertinence and rationality; its predecessors for the most part struck me as ill-considered, ill-tempered, and ill-informed. They were also accompanied by a campaign of suppression, distortion, and intimidation. Under such circumstances, I have no alternative but to oppose myself to the 99-and-some-fraction per cent of American scientists who believe the issue to be closed.

Though I am not a Velikovsky disciple, I am prepared to be held accountable for my belief that he has not been fairly dealt with by the academic community. *Harper's* allowed him the "last word" only as it would any of its authors who was under fire. I am in debt to the editor of SCIENCE for permitting me the same, though I doubt that the controversy is quite as dead as Dr. Schafer suggests.

ERIC LARRABEE

New York City

Received May 8, 1953.

Removal of the Impurity in Bovine Serum Albumin and Its Effect on Zinc Binding[1]

IT has recently been reported in this journal by Feldman and Havill (*1*) that Armour's bovine serum albumin contains citrate as an impurity. The existence of a non-protein impurity has been known in this laboratory for some time, and, since its probable identification as citrate must throw some doubt upon the validity of metal binding studies previously reported from this laboratory (*2*), a preliminary report of some experiments performed with bovine serum albumin from which this impurity has been removed would seem to be indicated.

Armour's bovine serum albumin was purified by passage of a concentrated solution through an ion exchange column, exactly as specified for human serum albumin by Oncley and Dintzis (*3*). Comparative citrate analyses, by the method of Saffran and Denstedt (*4*), indicate that at least 90% of the impurity has been removed.

Titration curves have been run both on the commercial and purified preparations. They indicate that the former contains about two extra carboxyl groups per mole. This figure is, within the experimental error, compatible with the presence of about 0.5 mole of citrate per mole of albumin. Most of this difference affects the titration curve acid to the iso-ionic point;

[1] This investigation was supported by a research grant from the National Institutes of Health, USPHS.

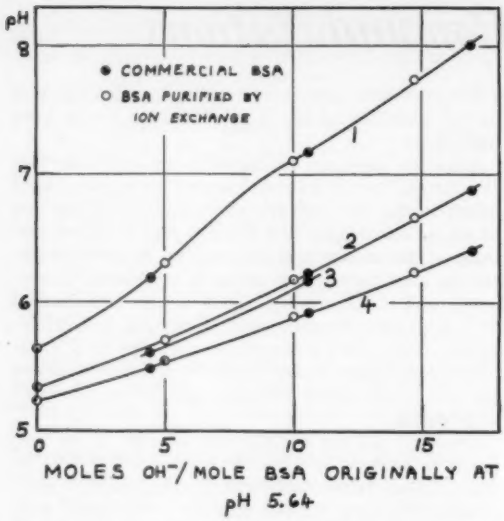

FIG. 1. Titration curves of bovine serum albumin (BSA). Curve 1—no added Zn. Curve 2—0.0025 *M* Zn. Curve 3—0.0029 *M* Zn. Curve 4—0.0075 *M* Zn. All solutions contained about 2.2% BSA and 0.15 *M* KNO_3. The molecular weight of BSA has been taken as 69,000.

between pH 5.6 and pH 9 the two titration curves are virtually superimposable.

An accurate way to observe differences between the purified and commercial preparations with respect to metal binding is to measure the effect of the metal ion on the titration curves. Large pH drops accompany the binding of metal (*5, 6*).

Figure 1 shows a portion of the titration curves of bovine serum albumin before and after purification, in the presence of 0.15 *M* KNO_3 and varying amounts of $Zn(NO_3)_2$. These curves show clearly that no appreciable difference has resulted from the removal of the impurity. It can therefore be concluded that the interpretation of metal binding studies on bovine serum albumin previously reported from this laboratory is not invalidated by the findings of Feldman and Havill.

A more complete study of the titration curves of bovine serum albumin is currently in progress and will be reported elsewhere at a later date.

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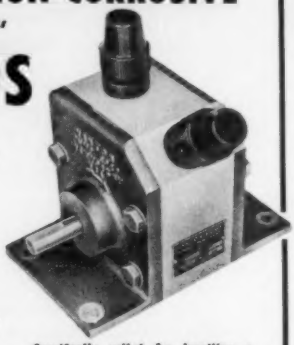

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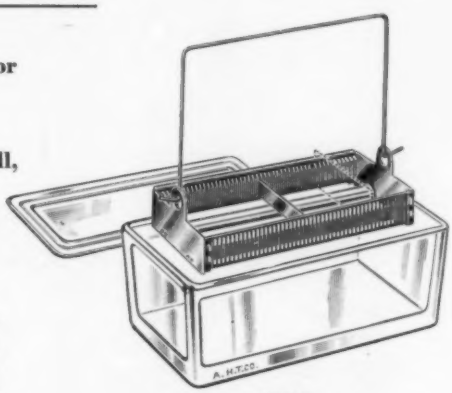

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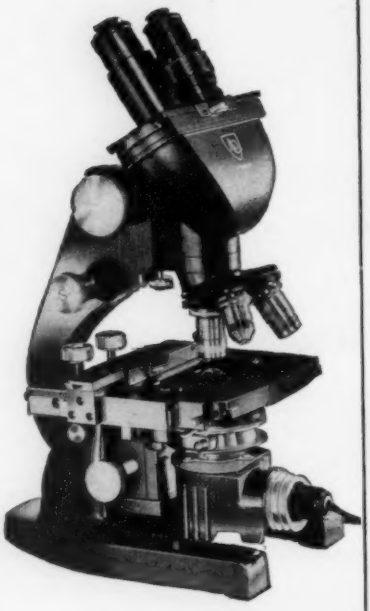

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